

## Feasibility Testing of Neurobic Exercise Intervention in Older Adults with Mild Cognitive Impairment

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### Abstract:

**Objective:** To explore the feasibility of neurobic exercise intervention among older adults with mild cognitive impairment (MCI).

**Material and Methods:** This pilot study used a two-group pre-post test, with a follow-up design. Older adults with MCI were randomly assigned to the intervention group (n=10) or the control group (n=10). Measurements included: the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) and the Common Objects Memory Test (COMT). Acceptability was assessed using a satisfaction and helpfulness rating scale and open-ended questions.

**Results:** The intervention group had a significant reduction in IQCODE relative change score, indicating improvement in cognitive decline, and had a significantly higher COMT relative change score, indicating improvement in cognitive performance at 3 and 6 weeks. Participants reported high satisfaction with the overall activities, and rated the intervention helpful.

**Conclusion:** The neurobic exercise intervention was feasible and acceptable for Thai community-dwelling older adults.

**Keywords:** feasibility, mild cognitive impairment, neurobic exercise, older adults

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## Introduction

Dementia is a decline in memory and other mental abilities, which is a significant health problem among older adults. Worldwide, the number of older adults with dementia will double within the next 20 years<sup>1</sup>. Additionally, it is estimated that dementia in older adults within Thailand will rise from 1.1 million in 2030, to 2.0 million by 2050<sup>2</sup>. Specifically, 71.4% of older people in Thailand have been diagnosed with mild cognitive impairment (MCI)<sup>3</sup>. MCI is an early stage of memory loss or other cognitive declines in individuals; however, they are still able to maintain the ability to independently perform most activities of daily living<sup>4</sup>. Part of the diagnosis of MCI, could be derived from memory performance based on self-reporting (subjective memory) or clinical assessment, or via standardized memory testing (objective memory)<sup>5</sup>. Older adults with MCI have an increased risk of developing dementia, especially Alzheimer's disease<sup>6</sup>. Thus, maintaining cognitive function early could delay brain degeneration including dementia in older adults. In addition, there is no specific medication treatment for MCI, therefore, nonpharmacological intervention could be an alternative treatment that could benefit patients with MCI.

The term 'neurobic' was first introduced by neurobiologists Katz and Rubin<sup>7</sup>. Neurobic exercises use the five senses; vision, smell, touch, taste, hearing, and emotional senses to enhance the brain's natural drive to form associations between different types of information<sup>7</sup>. Neurobic exercise is a scientific evidence-based intervention for brain exercise or cognitive training to keep the brain active and healthy<sup>8</sup>. This exercise involves taking the human brain out of its comfort zone by exposing it to new sensations or challenges outside of normal routine. Neurobic exercises can stimulate different parts of the brain and help prevent memory performance decline in addition to maintaining a continuing level of memory performance. It stimulates nerve cells to produce neurotrophins, which have

a chemical effect on the growth of nerve cells, increase the branching of nerve fibers and reduce the degeneration of nerve cells, which can enhance memory retention<sup>7,9</sup>. Neurobic exercises can help activate neural systems, increase blood supply to the brain as well as enhance nerve impulses and interconnections among different data within the brain<sup>10</sup>. In older adults with MCI, the neurobic exercise has been reported to delay the decline in cognitive function and to have positive impacts on the outcome variables of daily living abilities, mood and memory<sup>11,12</sup>.

Humeidan and colleagues conducted a randomized clinical trial (RCT) among older adults undergoing major, noncardiac and non-neurological surgery (n=268)<sup>13</sup>. Patients randomized into the neurobic exercise group had lower delirium incidence than controls at seven days post-operation. In a small RCT among patients with stroke (n=40), patients in the neurobic exercise group had significantly improved cognitive function and quality of life at four weeks post-intervention than controls<sup>14</sup>. Notably, in a two-group post-test design (n=60) the neurobic exercise intervention showed reduced depression scores among the older adults who had multiple comorbidities at one-month post-intervention compared to the controls<sup>15</sup>.

In Thailand, a few studies have been published testing the efficacy of neurobic exercise among older adults during hospital admission, and within communities. A single-group post-test design among 22 females with dementia showed an improvement in memory measured by the Mini-Mental State Examination score one month after completing the neurobic exercise intervention<sup>10</sup>. Another study of older adults with mild dementia (n=34) reported significant short-term memory improvement among participants at 3-month follow-up<sup>16</sup>. Additionally, Napatpittayatorn and colleagues tested the effect of neurobic exercise in a small RCT (n=51). The results showed that participants in the intervention group had improved cognitive function and serum brain-derived neurotrophic factor 6 months after

the intervention completion than controls<sup>9</sup>. Furthermore, using a non-randomized two-group post-test design among patients with type 2 diabetes mellitus (n=120), the patients in the intervention group reported a significant improvement in short-term memory scores than the control group at three months follow-up<sup>17</sup>. Another study among older community-dwellers with MCI (n=60) reported lower depression scores two months after completing the neurobic exercise intervention<sup>18</sup>.

Despite evidence of the benefits of neurobic exercise interventions, most previous studies targeted healthy, older adults or those with chronic illnesses. Very few studies have focused on older adults with MCI. Hence, his pilot study aimed to test the neurobic exercise intervention and evaluate the feasibility of a 3-week neurobic exercise intervention for older adults with MCI within a rural community in Thailand.

### Conceptual framework of the study

The concept of mild cognitive impairment<sup>5</sup> and neurobic exercise<sup>7</sup> were used to guide the design and intervention of this study. MCI is a transitional state between normal aging and dementia, characterized by an impairment of memory or another cognitive decline, which does not affect a person's basic activities during daily living<sup>5,19</sup>. Neurobic exercise is a brain exercise using five multisensory associations of physical senses (vision, hearing, smelling, tasting, and touching), and emotional senses to keep the brain active and healthy<sup>7</sup>. The neurobic exercise stimulates the brain with non-routine or unexpected experiences using various physical and emotional senses combinations. Thus, it is postulated that implementing neurobic exercise in older adults with MCI could improve cognitive function/memory, task performance and creativity, even at advanced age<sup>5,7,9</sup>.

### Purpose

This proposed study used a two group pre-post test, with a random assignment to compare the neurobic

exercise intervention with the control group that received standard care services. The feasibility and acceptability of the neurobic exercise intervention were evaluated. This paper followed the guidelines for publishing pilot study results<sup>20</sup>. The priori directional hypotheses and research questions were:

Hypothesis 1. The neurobic exercise intervention group participants would have a significantly lower score of cognitive decline (subject memory), measured by the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), than the control group at 3-weeks and 3-weeks post-intervention.

Hypothesis 2. The neurobic exercise group would have a significantly higher cognitive performance score (objective memory), measured by Common Objects Memory Test (COMT), than the control group at 3 weeks and 6 weeks post-intervention.

Research questions. Additional research questions were used to determine the feasibility of the neurobic exercise intervention: (1) Did the older adults completing the neurobic exercise rate the intervention as helpful in maintaining their memory? (2) What were the participant recruitment, enrollment and retention rates to determine future recruitment strategies, and understand the reasons for non-participation to be used in a more extensive study.

## Material and Methods

### Design

This study used a two-group pre-post test, with a follow-up design. Older adults with MCI were randomly assigned to the neurobic exercise intervention (n=10) or the control group (n=10). The feasibility of the intervention was evaluated in terms of recruitment rate, the number of sessions attended, retention rate and any adverse events. Acceptability was assessed using a satisfaction and helpfulness rating scale coupled with open-ended questions.

**Sample and setting**

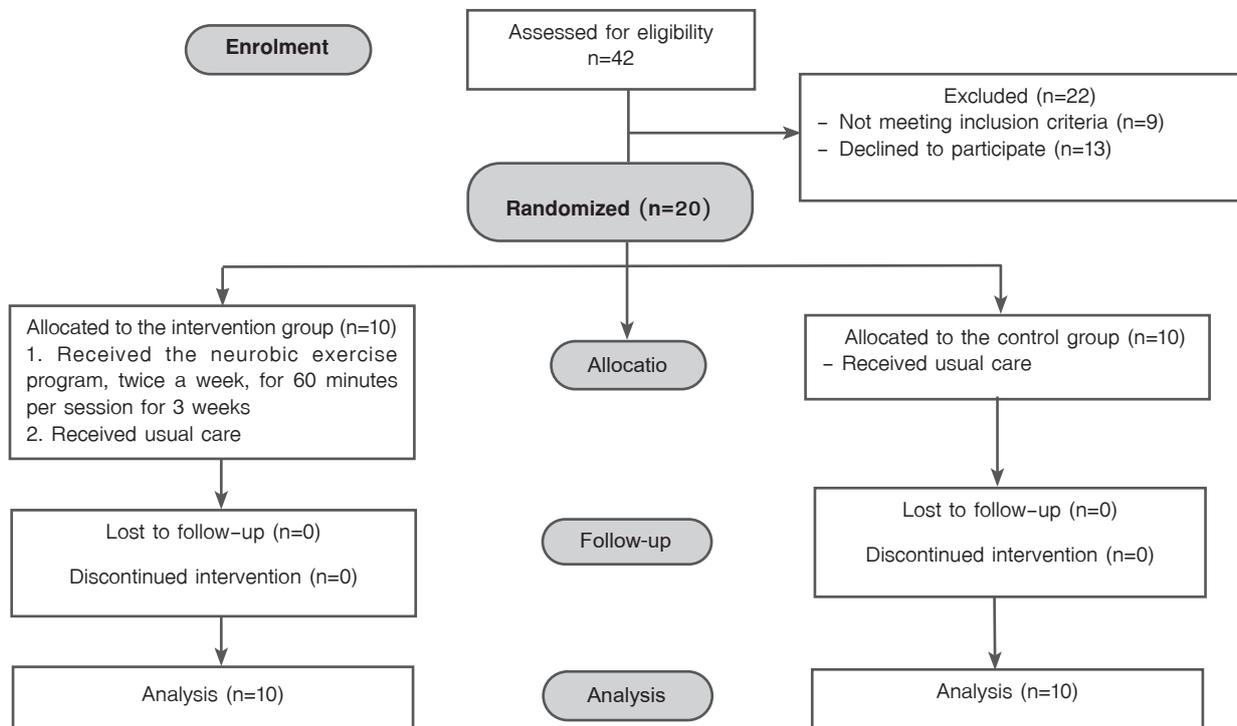
Sample: Participants were included if: they were 60 years old or above<sup>21</sup>, had a MCI (Montreal Cognitive Assessment (MoCA) score <24). Participants could have either amnesic or non-amnesic MCI, and were able to independently perform daily life activities without difficulty (Modified Barthel ADL index (BAI) ≥12), Body Mass Index (BMI) score range: 18.49–34.90 kg/m<sup>2</sup> (normal to Obesity Class I); able to read, write and speak Thai, and provided consent to participate. Excluded were older adults with a disability that precluded them to participate in the study (i.e., hearing, or visual impairment), and those with limited mobility (i.e., BMI over 35 kg/m<sup>2</sup>). Participants with a history of psychiatric disorders, neurological conditions, and food or flower allergies were also excluded.

Setting: The study was conducted at the senior club of Saraburi Hospital, located in Muang district of Saraburi

province, Thailand. The club was adjacent to the main hospital, providing extended community services for older adults in the Saraburi municipal area.

**Procedure**

Research Ethics Committee of Burapha University (IRB3-011/2564) approved the current study in addition to the Ethical Committee of Saraburi Hospital (EC002/2564). The trained research assistant (RA) explained the study to the participants. Once the older adults agreed to participate, the RA conducted screening per the inclusion criteria. Those meeting the eligibility criteria were enrolled and signed consent to participate. Each participant was randomly assigned (1:1 ratio) to either the intervention group (n=10) or the control group (n=10) using a computer-generated random table. The flow diagram of the selection procedure is presented in Figure 1.



**Figure 1** Flow diagram of the selection procedure

**Table 1** The six sessions of the neurobic exercise intervention

Session	Activities	Rational
Session 1: Visual Sense Stimulation	<p>Introduction the participants in the group to the neurobic exercise involving 5 senses, using a game form.</p> <ol style="list-style-type: none"> <li>1. The interventionist provided fifty minutes for psychoeducation on "Neurobic exercise for older adults with MCI" and fifty minutes for group discussion on "How to use the neurobic exercises in your daily life"</li> <li>2. Playing a tray game: the interventionist placed ten common household items (i.e. spoon, glass, etc.) in the tray and asked participants to look and remember the items within a set time (1 minute), then covered these items with a cloth.</li> <li>3. Participants were asked to recall all items by placing the matched pictures they recalled in front of them.</li> <li>4. The research assistant (RA) tallied the correct number of recall items.</li> <li>5. The interventionist removed three items and asked the participants to place the pictures of the missing items.</li> <li>6. The RA tallied the correct answers.</li> </ol>	The visual sense activities stimulated short-term memory, which is controlled by the occipital lobe, thalamus and hypothalamus.
Session 2: Smell Sense Stimulation	<ol style="list-style-type: none"> <li>1. The interventionist used natural aroma (candle) to help participants sit in a comfortable, relaxing position for five minutes.</li> <li>2. With their eyes closed, participants were asked to smell flowers and Thai herbs within the time set.</li> <li>3. Each participant smelled four different scents (two flowers and two Thai herbs).</li> <li>4. Participants were asked to guess each item and wrote it down on paper, with their non-dominant hand, within the time set (1 minute).</li> <li>5. The RA tallied the correct answers.</li> </ol> <p>Upon completing the visual and smell sense activities, the interventionist summarized how to use or apply visual and smell stimulation in their daily life.</p>	This smell sense activity stimulated the olfactory nerve that directly connects to the cortex, hippocampus and other parts of the limbic system involved in processing emotions and storing memories.
Session 3: Hearing Sense Stimulation	<ol style="list-style-type: none"> <li>1. Participants were asked to close their eyes and listened attentively to three different nature sounds (tidal waves, waterfall, birds singing).</li> <li>2. Participants were asked to guess each sound and wrote it down on paper within the time set (1 minute).</li> <li>3. The participants were asked to close their eyes again and listened to a combination of music, while listening to several natural sounds (bell ring, thundering, tidal wave, waterfall, birds singing) with closed eyes.</li> <li>4. Participants were asked to identify each sound that they heard and wrote it down on paper within the time set (1 minute).</li> <li>5. The RA tallied the correct answers.</li> </ol>	This hearing sense activity stimulated the temporal lobe and limbic systems that store memories of emotion and motivation. Also, listening to music increases neurotransmitter dopamine.
Session 4: Touch Sense Stimulation	<ol style="list-style-type: none"> <li>1. All participants were divided into three groups (3-4 persons/group), and one member of the group received the words (five short words) from the interventionist.</li> <li>2. The first participant from each group had read and remembered the word.</li> <li>3. They used a finger to write the word on the back of the next person in the group, and the next person did this until the last person.</li> <li>4. The last person in the group guessed what the word was and wrote that word on paper within the time set.</li> <li>5. Playing a puzzle box game, the participants touched five items inside a box with their non-dominant hand, while closing their eyes.</li> <li>6. Participants were asked to guess each item and wrote it down on paper within the time set (1 minute).</li> </ol> <p>Upon completing the hearing and touch sense activities, the interventionist summarized how to use or apply hearing and touch sense stimulation in their daily life.</p>	The touch sense activity activated the frontal and parietal lobes. The frontal lobe is essential for cognitive functions and plays an important part in processing both short-term memories and the retention of longer-term memories.

Table 1 (continued)

Session	Activities	Rational
Session 5: Taste Sense Stimulation	<ol style="list-style-type: none"> <li>1. With their eyes closed, participants were asked to taste fruit and vegetables in several flavors: sweet, sour, flavorless, salty and bitter tastes.</li> <li>2. Participants were asked to guess each item and wrote it down on paper, with their non-dominant hand, within the time set (1 minute).</li> <li>3. The participants were asked to close their eyes again and tasted food and desserts.</li> <li>4. Participants were asked to guess the name of food and desserts and wrote it down on paper with their non-dominant hand.</li> <li>5. For the food or dessert ingredients, they could mark the crosses on the answer sheet with their non-dominant hand.</li> </ol> <p>Upon completing the taste sense activities, the interventionist summarized how to use or apply visual and smell stimulation in their daily life.</p>	The taste activity affects the ability to retrieve memories. Also, it stimulates the frontal lobe, which controls essential cognitive skills; such as emotional expression, problem-solving, memory, language and judgment.
Session 6: Integration of multi-senses; Application in daily day usage.	<ol style="list-style-type: none"> <li>1. All participants were divided into two groups to compete in a cooking game.</li> <li>2. Each group created a menu, plans, and managed the time and money within the time set (10 minutes).</li> <li>3. Each group cooked its menu within the time set (20 minutes).</li> <li>4. Participants presented their menu and summarized how to plan and manage the group.</li> </ol> <p>Upon completing the last week of intervention, the interventionist answered any questions and summarized how to use or apply neurobic exercise in their daily life. Then, all participants completed satisfaction and helpfulness rating scale.</p>	Combining two or more senses involves processing short-term memories and retaining longer-term memories.

**Neurobic exercise intervention**

The researcher developed the neurobic exercise intervention based on previous evidence-based research<sup>7,9,10</sup>. The intervention manual was validated for content, process and implementation by five experts; including a psychiatrist, psychologist, neurologist and two nursing instructors from the gerontological and psychiatric mental health nursing departments. Minor modifications were recommended to ease the appropriate task for older adults. Furthermore, the researcher tested the instructions written in the manual with 20 older adults for understandability and difficulties. All 20 participants were able to follow instructions and completed both the study instruments and questionnaires without any difficulty.

For this study, all participants received standard usual care from health care providers; such as routine

treatment, education and counselling. Participants continued to engage in their everyday activities within their senior club; such as 30-minute morning aerobic exercise offered five days per week. Participants in the intervention group received 6 sessions of the neurobic exercise designed to enhance brain activity and health, which were delivered twice weekly for three weeks (6 sessions). Participants joined the group session, approximately 3-4 persons per group, with each session lasting approximately 60 minutes. The intervention involved stimulating one or more senses in a novel context. Specifically, participants were trained to practice various activities beyond their daily routine; such as: (1) observing key people’s characteristics in the news (i.e., the prime minister or Thai Royal families); (2) smelling objects in their house (flowers or Thai herbs), while closing their eyes then guessing what the objects were, (3) closing

their eyes and listening to several sounds (animal or natural sounds) then identifying what they were, (4) touching an object with a non-dominant hand then identifying what it was; and (5) closing their eyes and tasting food or desserts of various flavors then naming or guessing the ingredients. The activities of the neurobic exercise intervention are described in Table 1.

At the end of each session, participants received «homework» of simple brain activities learned from the group session to practice at home. Furthermore, at the beginning of the next session, participants were asked to discuss their 'homework' and share what they learned with the group.

### Instruments and questionnaires

Subjective memory was a self-report of how each participant interpreted, felt, thought, and perceived changes in memory problems and complained about their memory problems, they then reported their perceived cognitive decline. Subjective memory was measured by the 16-item Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), developed by Jorm<sup>22</sup>, and translated into the Thai language by Senanarong<sup>23</sup>. Participants compared their memory performance with the previous performance. Participants responded to the following questions: Compared with ten years ago, please indicate the changes you have observed by circling the appropriate answer. Sample questions were: (1) "Remembering things about family and friends: e.g., occupations, birthdays, addresses". (2) Remembering things that have happened recently. The response options ranged from much improved (score=1) to much worse (score=5). The sum scores across 16 items were then calculated. Higher scores on IQCODE indicated greater cognitive impairment. The Cronbach's alpha reliability score of IQCODE for this sample was 0.94.

Objective memory refers to memory or cognitive functioning testing that is not dictated by a state of emotions

or personal prejudices of one's memory. This study used a standardized Common Objects Memory Test (COMT) to measure object memory. The COMT<sup>24</sup> included repeated presentations of color photographs containing 10 common objects (button, chair, clock, comb, cup, key, knife, leaf, scissors and umbrella) and multiple opportunities for participants to recall and recognize the original list. The author and a bi-lingual researcher translated COMT manual instructions into Thai using a translation and back-translation method<sup>25</sup>. The translation achieved 100% inter-rater agreement. The COMT (Thai version) was tested with five older adults to ensure familiarity with the common objects and the distracters.

The COMT was conducted in 3 steps. In the first step (the learning step), the RA presented one picture at a time and asked the participant to name the objects aloud, and try to remember them. The RA confirms or corrects the answer of the participants and records the objects correctly recalled. These object recalls were repeated three times; thus, the possible range of scores was 0 to 30.

In the second step, the recall and recognition tests were administered at 5-minute delay intervals, which were filled with unrelated test activities (i.e., coloring the pictures). Each participant was asked to recall the ten objects again, and the RA recorded the number of objects recalled correctly. Then, the RA showed 20 photographs that included the 10 original objects and 10 new objects (hairbrush, purse, comb, lock, matches, spoon, book, telephone, fan and clothes pin). The participant looked at 20 pictures and indicated whether an object had been seen previously. The final score represents the number of objects correctly recognized. The possible range of scores was 0 to 30, including 10 scores for recalls and 20 scores for recognitions.

In the third step, another recall and recognition test were administered at 30-minute intervals, which were again filled with more unrelated test activities. The procedure and

recorded score were the same as described in the second step. The total sub-score was 30; including 10 scores of recalls and 20 scores of recognitions. Then the total COMT scores were summed across these three steps: the possible range being 0–90. Higher scores indicated better memory performance. Test–retest between time 1 and time 2 during the learning step of this study was 0.78 ( $p$ -value<0.001).

A Satisfaction and Helpfulness rating scale was used. Upon completion of the intervention, each participant rated their anonymous satisfaction and helpfulness of the neurobic exercise on a 7-item Likert-type short survey. Sample questions were: (1) Are you satisfied with the neurobic exercise? (2) Were the neurobic exercise sessions helpful to you? Response options ranged from very dissatisfied/not helpful (score=1) to very satisfied/helpful (score=5): possible ranges in score being 7 to 35. At the end of the survey, the participants were asked to share their opinions on open-ended questions; such as: "Please explain how the intervention was helpful. If the answer was not helpful, please explain why not?" "What do you suggest to improve this neurobic exercise?"

Demographic variables included age, gender, marital and living status, education level, occupation, income and if they were taking any medications for other health/illness conditions. The RA collected and confirmed participants' current weight and height for BMI calculation.

#### Data collection

Data were collected from all older adults with MCI in the intervention and standard care groups at baseline, 3 weeks (at the end of the intervention), and 6-week follow-up. The data were gathered on questionnaires that were completed in 45 to 50 minutes. The data collector was a trained research nurse, blinded to the random assignment.

#### Data analysis

Descriptive statistics were used to summarize the sample demographics and the neurobic exercise intervention evaluation data. Percent relative change scores from baseline to 3-week and 6-week outcome measures were calculated; for example, percent relative change score at 6 weeks was calculated by [(6-week score minus baseline score) divided by baseline score; multiplied by 100]. Relative change scores consider the degree of observed change score relative to the severity at baseline<sup>26</sup>. The outcome data had a normal distribution. Therefore, an independent t-test was used to detect a significant difference in relative changes in subjective (IQCODE) and objective memory (COMT) between groups (Hypothesis 1 and 2). Bonferroni's adjustment was calculated by taking the number of tests and dividing it into the alpha value (Armstrong, 2014). Thus, using the 5% error rate, two-sided t-tests ( $0.05/2$ ) would yield an alpha of 0.025 on each side. The anonymous open-ended survey data related to the satisfaction and helpfulness of the intervention were summarized and reported. All statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM). Cohen's d statistics (Cohen, 1988) was used to detect the effect size, which determined the magnitude of the difference between the two groups,  $d=0.2$  (small);  $d=0.5$  (medium); and  $d=0.8$  (large).

## Results

#### Demographic

There was no statistical significance in baseline demographics between the intervention and standard care groups. All participants met the screening criteria. The overall mean MoCA score was 20.50 (S.D.=2.85, range 13–24), ADL score was 19.65 (S.D.=0.58) and BMI was 24.34 (S.D.=4.09). Participants' mean age was 75.10

years (S.D.=5.65, range 64–84), 75% (n=15) were female, 40% (n=8) were married and 95% (n=19) lived with family members at home. Ten participants (50%) did not work, 45% (n=9) had retired with a government pension and one was employed. The average income for this sample was 16,275 (S.D.=16,841, range 600–50,000) baht per month. Notably, all participants aged 60 and above were eligible for

the state pension for older adults (beginning at 600 baht per month). For example, participants who were 60 years old and did not work reported 600 baht as their state pension monthly income. Of 20 participants, 80% (n=16) reported having other chronic illness conditions, such as hypertension 60% (n=12), dyslipidemia 55% (n=11), diabetes 20% (n=4), stroke 10% (n=2) and heart disease 5% (n=1); whereas, 62% (n=10) reported more than one condition (Table 2).

**Table 2** Baseline demographic characteristics of older adults with MCI participants (n=20)

Characteristic	Total sample (n=20)		Intervention (n=10)		Standard care (n=10)		t/x <sup>2</sup>	p-value
	n	%	n	%	n	%		
Age (range 64–84 years)	75.10 (5.65)		75.10 (5.68)		75.10 (5.93)		0.000 <sup>a</sup>	1.000
Income** (range 600–50,000 baht/month)	16,275 (16,841.04)		14,720 (16,351.33)		17,830 (18,055.90)		0.404 <sup>a</sup>	0.691
Gender							0.267 <sup>b</sup>	0.606
Male	5	25	2	20	3	30		
Female	15	75	8	80	7	70		
Marriage status							0.343 <sup>b</sup>	0.842
Single	5	25	2	20	3	30		
Married	8	40	4	40	4	40		
Divorced/widowed	7	35	4	40	3	30		
Education level							5.500 <sup>b</sup>	0.240
Less than high school	8	40	5	50	3	30		
Completed high school	4	20	1	10	3	30		
Vocational/technical	2	10	2	20	0	0		
Bachelor's degree	4	20	2	20	2	20		
Graduate degree	2	10	0	0	2	20		
Chronic illness							1.250 <sup>b</sup>	0.264
No	4	20	1	10	3	30		
Yes	16	80	9	90	7	70		

\*p-value<0.01, <sup>a</sup>=t-test, <sup>b</sup>=chi-square

\*\*The state pension for older adults (beginning at 600 baht/month) was provided by the government. Ages 60–69 receive 600 baht/month, 70–79 receive 700 baht/month, 80–89 receive 800 baht/month, and those aged 90 and above receive 1,000 baht/month<sup>33</sup>  
MCI=mild cognitive impairment

**Table 3** Comparison of percent relative change mean scores between groups at baseline, 3-week, and 3-week post-intervention

Variables	Intervention group M (S.D.) Min-max			Standard care group M (S.D.) Min-max			Percent relative change (%)		Cohen's d		Between-group Comparison	
	Baseline (T1)	3-week (T2)	6-week (T3)	Baseline (T1)	3-week (T2)	6-week (T3)	T2 & T1 (%)	T3 & T1 (%)	T1 & T3	Effect size	t	p-value
IQCODE <sup>b</sup>	53.40 (10.29) 32-68	51.60 (9.65) 30-64	51.40 (9.50) 30-64	51.40 (8.23) 30-58	52.70 (8.42) 33-64	53.10 (8.41) 33-64	-3.31	-3.62		0.18	3.67 <0.01	4.29 <0.001
COMT <sup>c</sup>	77.50 (3.50) 69-82	83.40 (2.11) 79-87	82.90 (3.57) 76-89	77.30 (8.35) 55-84	77.40 (8.38) 55-84	77.40 (8.34) 55-84	7.72	7.04		0.85	-7.13 <0.001	-5.44 <0.001

<sup>a</sup>Percent of relative change scores from baseline to 6-weeks=[(6-week score minus baseline score)/baseline score x 100]

<sup>b</sup>IQCODE<sup>b</sup>=subjective memory, higher scores=more cognitive decline

<sup>c</sup>COMT<sup>c</sup>=objective memory, higher scores=better memory performance

<sup>d</sup>Cohen's d=M1-M2/spooled, where spooled= $\sqrt{(s_1^2 + s_2^2)/2}$ ; which was: "small," d=0.2; "medium," d=0.5; and "large," d=0.8

### Effects of neurobic exercise on subjective memory

Compared to standard care, there was a significant reduction in IQCODE relative change score, indicating improvement on cognitive decline at 3 weeks (3.31% vs 2.75%), t=3.67 (p-value<0.001) and 6 weeks (3.62% vs 3.52%), t=4.29 (p-value<0.001); with small effect size (d=0.18). See Table 3. In addition, within-group differences were statistically significant when measured at different time points.

### Effects of neurobic exercise on objective memory

Compared to standard care, the intervention group had a significantly higher COMT relative change score, indicating improvement on cognitive performance at 3-weeks (7.72% vs 0.12%), t=-7.13 (p-value<0.001) and 6-weeks (7.04% vs 0.13%), t=-5.43 (p-value<0.001); with large effect size (d=0.85). See Table 3. In addition, within-group differences were statistically significant when measured at different time points.

### Additional research questions

Research question 1: Evaluation of the satisfaction and helpfulness of the neurobic exercise intervention. At 3 weeks after the completion of the neurobic exercise intervention, all ten participants in the intervention group completed the 7-item satisfaction and helpfulness scale. Participants highly rated the neurobic exercise intervention: The mean score was 30.80 (S.D.=1.87, range 28-33). All participants were highly satisfied with the overall neurobic exercise activities. They rated the intervention as helpful, and they could use them in their daily activities.

Based on the responses to the open-ended questions, participants reported all activities suitable for their age and health conditions. They said they enjoyed spending time with others in small group sessions. They

encouraged each other during the game sessions; for example, one participant mentioned: "I feel excited and enjoy the activities with my friends". Another participant said: "I think the activities are appropriate for my group and make me alert to do something new".

Notably, some participants stated that using their non-dominant hand and identifying objects with closed eyes was difficult. For example: "It was hard trying to mark the answers on paper with my left (non-dominant) hand". Another example was: "It was hard (from the beginning) to guess while closing my eyes and touching an object with a non-dominant hand in the time set".

Overall, participants were satisfied with the neurobic exercise; they enjoyed group participation and found it was helpful to stimulate their brains and improve memory. Some participants requested copies of their answers as references as well as additional score sheets to take home and practice with their family members. Upon the completion of each intervention session, participants were encouraged to monitor their improvement over time.

Research question 2: Evaluate participant recruitment, enrollment, and retention rates. There were approximately 500, older adults registered in the senior club of Saraburi Hospital; however, the activities in this senior club were suspended due to the COVID-19 pandemic, and only those with complete vaccination could join the activities in the senior club. This COVID-19 restriction had an impact on participant enrollment in this study. After the public broadcast at the senior club and bulletin board notice, only 42 older adults showed interest in participating. Of these 42, thirty-three older adults met the inclusion criteria. From this 33 older adults, who were eligible, 20 were enrolled, and 13 refused to participate due to scheduling conflicts, making them unable to attend and complete the 3-week intervention. Some participants had other home commitments, i.e., provided caregiving for their grandchildren at home, or already had travel plans to visit

their families in another province. Notably, 20 older adults signed the informed consent to participate (100% enrollment rate) and completed the study at 6-week follow-up. None of the participants in both groups withdrew during intervention implementation (three weeks for six sessions), indicating a 100% retention rate.

## Discussion

The result of this pilot study showed that participants in the neurobic intervention group had improvement in both subjective memory (IQCODE) and objective memory (COMT) after completing the neurobic exercise at 3 and 6-week follow-ups. The results aligned with previous studies that combined cognitive training activities that effectively stimulated memory and maintained cognitive functions in older adults<sup>27,28</sup>.

Neurobic exercise is a good brain exercise, designed to help the brain be active and healthy. It uses the six senses and breaks routine activities to strengthen nerve cell stimulation<sup>7</sup>. Routine activities can be 'brain deadening', because routine behaviors use the same brain pathways. Five physical senses and emotional senses helped activate the prefrontal association cortex part of the brain responsible for creating memory in addition to stimulating the hippocampus and limbic (emotion and motivation) system to improve memory function<sup>7,9</sup>.

Specifically, the neurobic exercise intervention used stimulating one or more senses in a novel context beyond the participants' daily routine, which increases connections between neurons in the brain. Each sense activates brain functions and nerve connections, which involve the memory process. As new experiences accumulated, the brain escalated continuous connections and pathways. This process could prevent any loss of the brain from being underused<sup>10</sup>. In this study, participants were asked to observe and name the key people characteristics in the news, i.e., the prime minister, and Thai Royal family

members. The activity stimulated the occipital lobe, which processed visual information and relayed sensory information to the cerebral cortex. The processing of semantics in vision plays a key role in forming long-term memory. This exercise helped participants recognize the face, names, and key characteristics of the people, helping them recall those people. Participants were challenged to complete the games (intervention) with their eyes closed to identify objects, and smell flowers, herbs and food via the use of their non-dominant hand to touch and identify objects. This exercise helped participants identify and differentiate common objects they saw in their own homes or local community. Smelling activates the temporal lobe, which plays an important role in the perception of odors that retain odor information of the objects, and enhanced odor memory processing. Using their non-dominant hand helped the brain to be active, think differently and become more creative.

In addition, the combination of two or more senses stimulates the brain's function, which involves the memory process; including: the frontal, parietal, temporal, occipital lobe, diencephalon and limbic systems. As a result, the neurobic exercises stimulated the function of neural networks involved in both short-term and long-term memory<sup>10,15</sup>.

Overall, the participants in this study highly rated the neurobic exercise intervention as helpful, and they were able to use it at home. The intervention was culturally appropriate to use for older Thai adults in the rural community. The participants reported that they felt relaxed and happy in the group, and they were likely to use this neurobic exercise beyond the intervention completion. These simple and fun activities use a game form that can be done anywhere, anytime and with other family members or grandchildren. Although, memory decline is common among older adults, approximately 18% of MCI could be reversed to normal cognition<sup>29</sup>. Thus, neurobic exercises could maintain brain

circuits as alerted and activated, which in turn improves memory retention among older adults.

This study also utilized both subjective and objective memory measurements. The MCI condition caused a slight, yet noticeable change in memory; however, this was not severe enough to affect the activities of daily living<sup>4</sup>. As a result, the subject's memory was mainly derived from self-reports or relatives, which varied considerably. Many people recognize memory decline as part of the aging process, and these people are less likely to get professional health educational advice. Clinicians could use clinical assessments with standardized memory testing (objective memory) to confirm an MCI diagnosis<sup>5,30</sup>, and then refer said older adults for further professional consultation, and neurobic exercises for early brain stimulation. Previous studies have reported subjective memory complaints as being associated with objective cognitive status, and also subjective memory complaints can predict conversion from normal cognition to dementia among the older population<sup>31</sup>. Thus, using the common IQCODE for subjective memory and COMP for objective memory measures would benefit early MCI diagnosis<sup>32</sup>.

In addition, these study results indicated the feasibility of neurobic exercise intervention for older adults in the community. The 100% enrollment rate and retention from baseline through till 6-week follow-up was achieved. Participants rated the intervention as helpful and easy to follow. They were likely to continue using it with their family members. Specifically, as shown in this study, neurobic exercises have potential benefits for older adults at early retirement age: 60 years old and above.

### Limitations

The small sample size, with predominantly female participants and short duration of intervention follow-up, were limitations of this study. However, the random assignment of the participants was a strength in reducing

biases in group assignments. Another limitation was due to the conduct of the study at only one senior club, under Saraburi Regional Hospital. These older adults at the senior club were more likely to be active and susceptible to learning new programs. In addition, the study was conducted from February to April 2021, and was impacted by COVID-19 restrictions. Only participants who received complete vaccination were eligible to enroll and participate in this study.

### Implications for future research

The results of this study showed promising, positive outcomes and benefits of neurobic exercises for older adults with MCI in the home and rural community. The effect size calculations from this pilot study can be used in power analysis and sample size determination for a larger longitudinal study<sup>20</sup>. Future studies with longitudinal follow-up to evaluate health outcomes of improved memory performance, such as life satisfaction, quality of life, healthy living, fall incidents, hospitalizations or emergency room visits are warranted. Subgroup analyses, such as testing differences between males and females on subjective and objective memory improvement could be conducted in a larger study<sup>10</sup>.

### Implication to practice

In addition to self-reporting (subjective memory), clinicians could use standardized clinical assessments (objective memory) to confirm an MCI diagnosis, and then refer said older adults for further professional consultation.

Step-by-step early brain stimulation, such as the neurobic exercise intervention could benefit older adults who have early signs of MCI.

Involving family caregivers or other community members in game-based brain exercises could be helpful to keep older adults enjoying activities within groups.

## Conclusion

This study indicates that the neurobic exercise intervention used a step-by-step, practical approach to enhancing memory performance. The results indicated that the neurobic exercise intervention was feasible and acceptable by Thai community-dwelling older adults. Both subjective and objective memory among older adults with MCI were improved at both 3 and 6-week follow-ups. Future longitudinal studies, with a larger sample size are warranted.

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