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# Tangram Puzzles in Patients with Neurocognitive Disorders: A Pilot Study

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**Abstract:** Objective: The tangram puzzle is a serious math puzzle game used to promote mathematic development in children, which improves visuospatial function and creativity. A game to improve cognitive functions is useful for patients with neurocognitive disorders. This pilot study aimed to determine whether this game could improve cognitive function in patients with neurocognitive disorders. Materials: This study recruited patients with mild Alzheimer's disease or mild cognitive impairment who were followed longitudinally by the Department of Psychiatry, Juntendo University Hospital, or Juntendo Tokyo Koto Geriatric Medical Center (Tokyo, Japan). Methods: Participants were asked to solve Tangram puzzles 2–3 times weekly, spending 30–40 min/session at home with or without family members for approximately 90 (Study 1) or 180 (Study 2) days. Mini-Mental State Examination (MMSE) in Study 1 as well as a Japanese version of the Montreal Cognitive Assessment and Trail Making Test in Study 2 were performed on the initial and final days. Results: Study 1 comprised eight participants and Study 2 comprised nine participants. Statistically significant improvement was observed in MMSE total score ($p = 0.016$) and orientation segment ($p = 0.026$) in Study 1. No statistically significant difference was noted in MMSE total score, orientation segment, or MoCA-J (Japanese version of Montreal Cognitive Assessment) score between the initial and final days in Study 2 ($p = 0.764$, $p = 0.583$, and $p = 0.401$, respectively). Conclusions: Study 1 revealed that Tangram puzzles may ameliorate the progression of cognitive functions in patients with neurocognitive disorders within a short time (3 months); however, Study 2 did not show a consistent result. Thus, randomized controlled trials are warranted to draw a conclusion.

**Keywords:** Alzheimer's disease; mild cognitive impairment; tangram puzzle; cognitive activity

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## 1. Introduction

Japan has over 36.23 million older people (aged > 65 years), accounting for 29.1% of the total population (1 October 2022) [1]. The number of older people with dementia in Japan is predicted to increase to approximately 6.75–7.30 million by 2025, with 1 in 5 people being aged > 65 years [2,3], imposing a heavy economic burden. In 2014, the national societal cost associated with dementia in Japan was estimated to be 14.5 trillion JPY (108 billion US dollars). Globally, 50 million people are suffering from dementia, with approximately 10 million new cases every year, and the cost of care for people with dementia is estimated to increase to 2 trillion US dollars annually in 2030 [4]. Patients with dementia also impose a heavy mental toll on family members, especially caregivers [5]. The caregivers' stress is related to the severity of dementia—the more severe the more stress [6]. Low-cost and accessible preventions and treatments for cognitive function loss are urgently needed with rising healthcare costs and increasing proportion of people aged > 65 years.

Mild cognitive impairment (MCI) refers to a transitional stage between normal cognitive aging and a more severe cognitive decline associated with dementia. Deterioration symptoms such as memory loss, inattention, and other cognitive decline are extremely common during this stage. A previous study showed that 10–15% of MCI cases progress to

dementia annually, thus preventing the progression of dementia is a major challenge [7]. Several treatments have been used to prevent the reduction of cognition, including pharmacological treatments such as galantamine or other acetylcholinesterase inhibitors, which are prescribed according to parient conditions, and nonpharmacological interventions such as autonomic training, antioxidant consumption [8], exercise (aerobic exercise), thinking processes, and social activities [9].

Alzheimer's disease (AD), one of the most common types of dementia, causes many debilitating symptoms in older individuals, especially those aged > 65 years. If this condition is diagnosed before the age of 65 years (uncommon), it is referred to as early onset AD (EOAD) or younger-onset AD [10]. The principal manifestations of AD-induced dementia include memory loss and disorientation with time and place. No curative pharmaceutical agents exist to treat these symptoms. Cholinesterase inhibitors (donepezil, galantamine, and rivastigmine) as well as memantine, an N-methyl-D-aspartate receptor antagonist, have been prescribed as common pharmaceutical treatments [11]. However, new medications such as aducanumab and lecanemab have been recently approved by the United States Food and Drug Administration for AD. Both of these drugs are humanized IgG1 monoclonal antibodies that bind to amyloid-β (Aβ) protofibrils and aggregated Aβ. However, compared with the time at which they were studied, there are no safety or effectiveness data on starting treatment at earlier or later stages of the disease [12]. The 2019 Risk Reduction of Cognitive Decline and Dementia World Health Organization guidelines mentioned that increased cognitive activity may stimulate (or increase) cognitive reserves and exert a buffering effect against rapid cognitive decline [13,14].

The tangram puzzle is a serious math puzzle game that has a history of over 1000 years in China. It is a highly playable game not only for children but also for adults. Currently, people in China utilize this game to improve children's intelligence, especially visuospatial mathematical intelligence [15]. Ayaz et al. examined the hemodynamic changes in the frontal region while solving computerized Tangram puzzles and revealed increased total hemoglobin levels in the right hemisphere [16]. Another research revealed that lower cerebral blood flow was associated with lower scores in the Mini-Mental State Examination (MMSE) [17] and that tangram puzzles increased the local cerebral blood flow.

Therefore, we hypothesized that tangram puzzles would help maintain patients' cognitive function, thereby delaying or even reversing cognitive decline. This pilot open-label, single-arm study examined whether tangram puzzles affect cognitive function in patients with early AD or MCI.

## 2. Materials and Methods

### *2.1. Participants*

In Study 1, patients who were diagnosed with mild AD with MMSE scores of 17–30 were recruited from the Department of Psychiatry, Juntendo University Hospital.

In Study 2, patients who were diagnosed with mild AD or MCI with MMSE scores of 17–30 were recruited from the Department of Psychiatry, Juntendo University Hospital or Juntendo Tokyo Koto Geriatric Medical Center (Tokyo, Japan).

Following the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, AD was diagnosed based on clinical interviews with at least three experienced psychiatrists. Written informed consent was obtained from all participants. Patients who could not understand this research and those with psychiatric complications were excluded from the study. None of the participants had a history of alcoholism or psychoactive substance abuse. All participants were prescribed appropriately before enrolment and were required to maintain the dose regimen during the observation period.

The Ethics Committee of the Juntendo University Hospital (18-108) approved the study, which was conducted in compliance with the guidelines of the Declaration of Helsinki.

### *2.2. Protocol*

Participants in Study 1 were asked to solve tangram puzzles 2–3 times weekly, spending 30–40 min per session at home with or without family members. The observation period was 90 days. The investigator established three groups of targets and paired three pamphlets with three sets of tangram puzzles (with same size but different colors). Target 1 (Figure 1) included geometric shapes (black) and number shapes (colorful). Targets 2 (Figure 2) and 3 (Figure 3) included animal shapes and common object shapes. In total, >100 instruction maps were used (target figures of tangram puzzles). Participants received a new target every 30 days. Further, the investigator recorded the MMSE score every 30 days, four times in total.

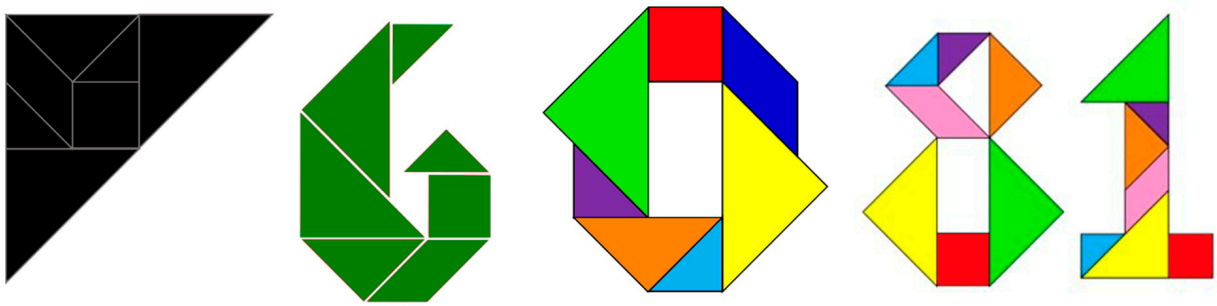


**Figure 1.** Instruction maps in Target 1.

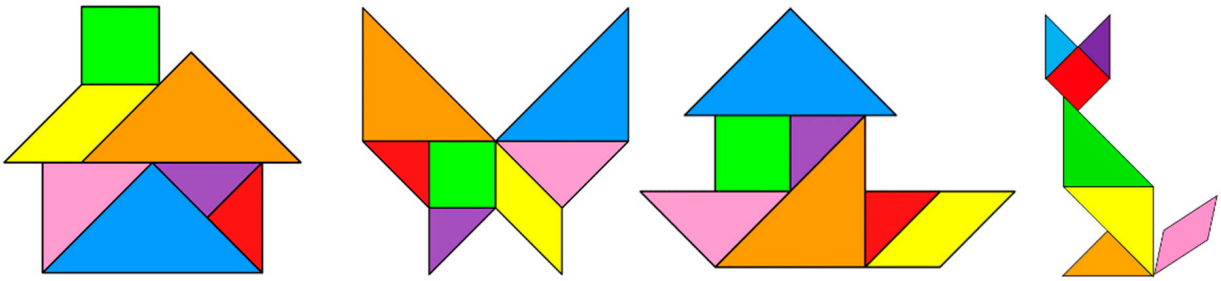


**Figure 2.** Instruction maps in Target 2.

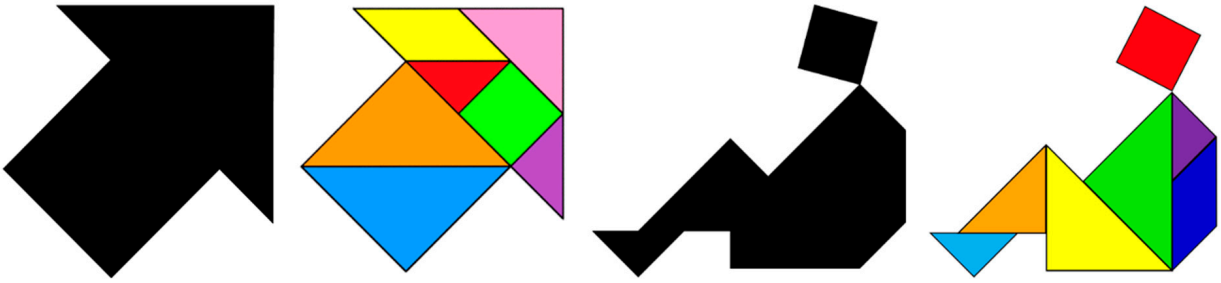


**Figure 3.** Instruction maps in Target 3.

Target 1 was utilized in the first month. Participants started solving the puzzle with geometric shapes (black patterns with gray outlines) in the first week, green number shapes in the second week, and colorful number shapes in third and fourth weeks.

Target 2 was utilized in the second month. There were 45 colorful instruction maps, comprising animal shapes and common object shapes.

Target 3 was utilized in the third month. A total of 20 instruction maps from Target 2 were laid out in the puzzle mode (black patterns without outlines). Participants were first asked to match a colorful instruction map and try to remember the locations of the seven pieces and then reconstruct them following the black pattern.

Participants in Study 2 were asked to solve tangram puzzles 2–3 times weekly, spending 30–40 min/session at home with or without family members for 180 days. Two sets of tangram puzzles (with same size but different colors) were provided. Different instruction maps were utilized every 2 months as described in the tangram task section below. The investigator described a new katakana version (Figure 4) to increase interest regarding the topic during treatment to better adapt to the Japanese culture. MMSE, Japanese version of the Montreal Cognitive Assessment (MoCA-J), and Trail Making Test (TMT) scores were recorded on the initial and final days.

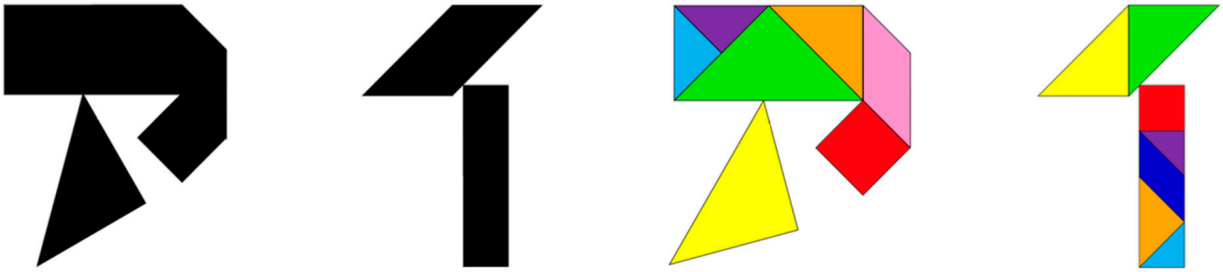


**Figure 4.** Instruction maps of katakana (T3/4).

### *2.3. MMSE*

The MMSE is a 30-point questionnaire that is extensively used in clinical and research settings to measure cognitive impairment and examine functions. It includes orientation (0–10), registration (0–3), attention and calculation (0–5), recall (0–3), and language and praxis (0–9) [18].

### *2.4. MoCA-J*

The MoCA is a neurophysiological test widely used to detect cognitive impairment [19]. This test consists of 30 points, including executive function/visuospatial ability (0–2), clock-drawing test (0–3), animal naming (0–3), short-term memory/delayed recall (0–5), attention (0–3), calculation (0–3), language (0–3), abstraction (0–2), and orientation (0–6).

### *2.5. TMT*

The TMT is a neurophysiological test used to assess intelligence; however, it is currently utilized to assess cognitive function. It is a timed test that involves visual scanning and working memory to evaluate the capability of maintaining visual attention and demonstrating "task switching." The TMT comprises two parts: TMT-A (attention and visuospatial function) and TMT-B (executive function) [20].

The Japanese version of TMT incorporated some changes to integrate it into the Japanese culture.

### *2.6. Tangram Task*

One set of tangram puzzles includes seven different color cardboards: two large isosceles right triangles, one midsize isosceles right triangle, two small isosceles right triangles, one square, and one parallelogram. Participants were asked to place the seven cardboards correctly to form a specified shape according to the instruction maps. The rule is that all seven pieces must be utilized, and no pieces should overlap.

### *2.7. Demonstration*

A face-to-face practice session of approximately 40 min between the investigator (also known as the trainer) and participant would be conducted on every patient visit day to determine whether participants and their family members solved the puzzle appropriately while maintaining patient adherence as much as possible.

The investigator selected an instruction map and one set of tangram cardboard, which were randomly shown to the participant. The participant was then allowed to place all

seven cardboard pieces at their appropriate location according to the instruction map (see Supplementary Materials).

The Target 1 instruction map was utilized in the first month of Study 1. Participants started solving the puzzle with geometric shapes (black patterns with gray outlines) in the first week, green number shapes in the second week, and colorful number shapes in third and fourth weeks.

After placing the target, the participants can attempt to initiate a conversation on a related topic (any associated memory or imagination) with the investigator or family members. This conversation should let participants recall their long-term memory or describe the image in their head in as much detail as possible, and unreal content need not be corrected.

The observation period in Study 2 was 180 days, indicating that participants required more instruction maps. Thus, the investigator described a new katakana version integrated Target 3 and named it as Target 3/4, which was utilized in third and fourth months. Participants completing the target could develop a "word game" such as "speak 10 words starting with ka." A different layout version of T3/4, known as T5/6, would be utilized in the fifth and sixth months.

### *2.8. Overall Procedure*

The observation period was 90 days in Study 1. The participants visited the mental clinic every 30 days. The investigator recorded MMSE scores on the initial day and next visit days until the 90th day. Participants received three sets of tangram puzzles and instruction maps (Targets 1, 2, and 3) in person and solved them at home with or without family members. Finally, participants were debriefed, acknowledged, and dismissed.

In Study 2, the observation period was prolonged to 180 days. MMSE, MoCA-J, and TMT data were recorded on the initial day. Participants visited the mental clinic and received instruction maps every 2 months (Targets 1/2, Targets 3/4, and Targets 5/6). MMSE, MoCA-J test, and TMT data were collected on the final day. Finally, participants were debriefed, acknowledged, and dismissed.

### *2.9. Statistical Analysis*

The chi-square test was used to assess differences in the frequencies of patient characteristics (e.g., sex) between Studies 1 and 2. Differences in MMSE score, MoCA-J score, and TMT-A/B ratio between the initial and final days of the study were examined using the Wilcoxon matched-pairs signed-rank test. All statistical analyses were conducted using Statistical Package for the Social Sciences version 22 software (IBM Corp., Armonk, NY, USA). A probability ($p$) value of $<0.05$ was considered to indicate statistical significance.

## 3. Results

Overall, 10 participants (7 males and 3 females) were recruited in Study 1. Two participants (No. 1 and No. 3) dropped out from the study because they had a family emergency or were too busy to receive training. Hence, eight participants completed the study (seven males and one female, Tables 1 and 2).

**Table 1.** Description of participants in Study 1.

| Variable | Participants ($n$ = 8) |
|---|---|
| Sex, M/F | 7/1 |
| Age, mean ± SD, years | 66.0 ± 12.3 (50–78) |
| Age of onset of AD (range), years | 63.3 ± 11.7 (49–77) |
| Duration of AD (range), years | 2.8 ± 1.8 (1–6) |
| Education (range), years | 14 ± 2.1 (12–16) |

**Table 2.** Details of participants in Study 1.

| No. | 2 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|
| **Sex** | M | M | M | M | M | M | M | F |
| **Age (y)** | 76 | 50 | 62 | 76 | 52 | 78 | 56 | 78 |
| **Onset (y)** | 73 | 49 | 61 | 72 | 49 | 77 | 53 | 72 |
| **Dur (y)** | 3 | 1 | 1 | 4 | 3 | 1 | 3 | 6 |
| **Edu (y)** | 12 | 16 | 16 | 12 | 16 | 12 | 16 | 12 |
| **Medication** | Donepezil hydrochloride | Donepezil hydrochloride | Memantine hydrochloride | Rivastigmine | Donepezil hydrochloride | Donepezil hydrochloride | Donepezil hydrochloride | Memantine hydrochloride |
| **Dosage** | 5 mg/QD | 5 mg/QD | 10 mg/QD | 9 mg/QD | 5 mg/QD | 3 mg/QD * | 5 mg/QD | 20 mg/QD |
| **Living with** | Spouse | Spouse | Spouse | Spouse | Spouse | Spouse | Spouse | Daughter |
| **Plays Tangram Puzzles with** | Self | Self | Self | Self | Self | Self | Self | Self |
| **Entertainment** | No hobby | No hobby | Walking | No hobby | Gym, climbing | Golf | Aerobic exercise | No hobby |
| **Alcohol Intake** | No | No | No | No | No | No | 500 mL/day ** | No |
| **Tobacco Use** | No | No | No | No | No | No | No | No |
| **Previous/ Present Career** | Unemployed | Engineer (still working) | Apartment supervisor | Chef | Mechanical design | Service industry | Office staff | Housewife |
| **Retirement (y)** | - | | 63 | 72 | 50 | 61 | 56 | - |

* The dosage of participant no. 8 was increased to 5 mg since day 61. For a new outpatient, the initial dosage regimen is started with 3 mg to check for any side effects. After the observation period (usually 1–2 months), the dosage is increased to 5 mg, which is a common dosage for patients with dementia. y: year; Dur: duration; Edu: education; QD: once daily, **: beer; -: stands for not reported.

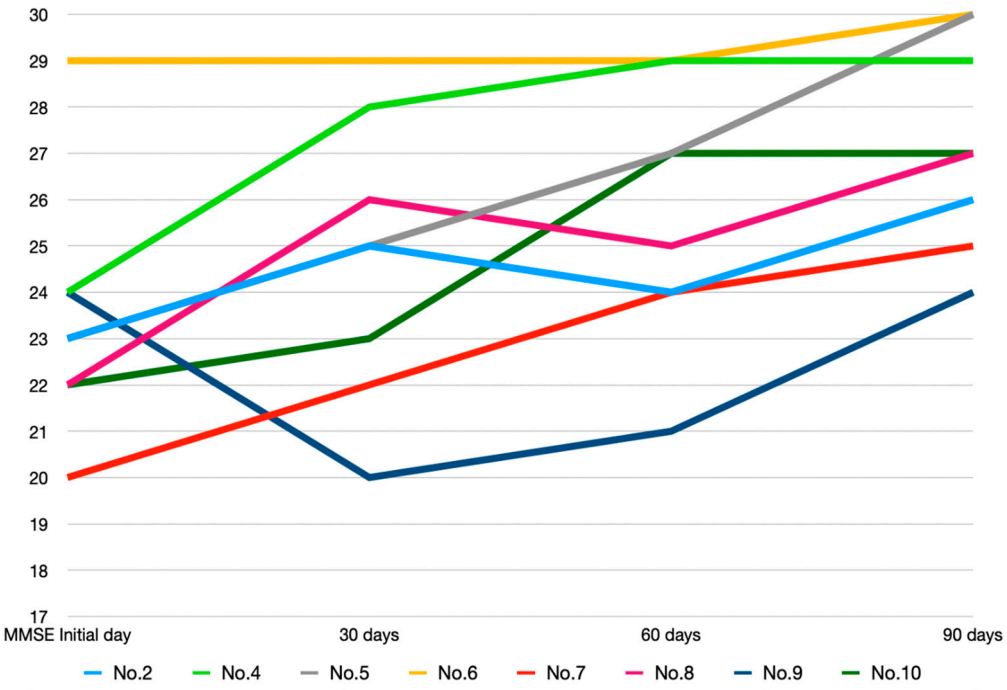
No adverse events were noted. Upon the completion of Study 1, none of the eight participants showed a decrease in MMSE scores. After 90 days, MMSE scores increased by $\geq$3 points in six of eight participants (Figure 5). Statistically significant improvement was observed in MMSE total score ($p$ = 0.016) and orientation segment ($p$ = 0.026). No statistically significant improvement was observed in registration ($p$ = 1.000), attention and calculation ($p$ = 0.066), recall ($p$ = 0.140), and language and praxis ($p$ = 0.102) (Table 3). Most participants reported enjoyment while solving the puzzle, and all participants experienced difficulty solving Target 3. Seven of the eight participants stated that they would play this game continually even after the completion of the study.

**Table 3.** Statistical analysis of cognitive outcomes based on MMSE scores in eight participants after 90 days in Study 1. Wilcoxon test.

| MMSE Score | Initial Day | Final Day | Z | *p* |
|---|---|---|---|---|
| Total | 23.4 ± 2.6 (20–29) | 27.3 ± 2.3 (24–30) | 2.4 | **0.016** |
| Orientation | 7.9 ± 1.6 (5–10) | 9.3 ± 1.4 (6–10) | 2.2 | **0.026** |
| Registration | 3.0 ± 0.0 (3) | 3.0 ± 0.0 (3) | 0 | 1.000 |
| Attention and calculation | 2.6 ± 1.5 (0–5) | 3.9 ± 1.5 (1–5) | 1.8 | 0.066 |
| Recall | 1.3 ± 1.2 (0–3) | 2.1 ± 1.1 (0–3) | 1.5 | 0.140 |
| Language and praxis | 8.5 ± 0.8 (7–9) | 9.0 ± 0.0 (9) | 1.6 | 0.102 |

*p*-values with statistical significance are indicated in bold. MMSE: Mini-Mental State Examination.

Although the results of Study 1 were provocative, we could not draw a conclusion because the duration of the intervention (90 days) was extremely short. We determined whether tangram puzzles could enhance cognitive function over an extended period. Therefore, we decided to perform Study 2, in which the duration of the intervention was prolonged to 180 days and cognitive function was assessed using multiple tools. To eliminate the possibility of retest effect in neuropsychological assessment, the results were recorded only twice: on the initial and final days.




| No. | MMSE Initial day | 30 days (Target 1) | 60 days (Target 2) | 90 days (Target 3) |
|---|---|---|---|---|
| **2** | 23 | 25 | 24 | 26 |
| **4** | 24 | 28 | 29 | 29 |
| **5** | 23 | 25 | 27 | 30 |
| **6** | 29 | 29 | 29 | 30 |
| **7** | 20 | 22 | 24 | 25 |
| **8** | 22 | 26 | 25 | 27 |
| **9** | 24 | 20 | 21 | 24 |
| **10** | 22 | 23 | 27 | 27 |

**Figure 5.** Changes in MMSE scores in patients with mild AD over 90 days.

Ten participants were recruited in Study 2. MMSE, MoCA-J, and TMT were performed on the initial and final days. One participant dropped out (participant no. 3) because the patient and his wife decided to visit another clinic. Thus, nine participants (two males and seven females, Tables 4 and 5) completed the study.

**Table 4.** Description of participants in Study 2.

| Variable | Patients ($n$ = 9) |
|---|---|
| Sex, M/F | 2/7 |
| Age, mean ± SD, years | 79.2 ± 3.1 (75–83) |
| Age of onset of AD (range), years | 75.4 ± 3.7 (70–80) |
| Duration of AD (range), years | 3.9 ± 2.7 (1–9) |
| Education (range), years | 13.1 ± 2.8 (9–16) |

AD: Alzheimer's disease.

No adverse events were noted. No statistically significant difference was observed in MMSE and MoCA-J scores between the initial and final days ($p$ = 0.764, $p$ = 0.401, Tables 6–8). No statistically significant difference was noted in any of the segments in MMSE. All participants reported enjoyment while solving Targets 1/2 and during short conversations but were frustrated when challenged in puzzle mode (Target 3/4, Target 5/6).

**Table 5.** Details of participants in Study 2.

| No. | 1 | 2 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| **Sex** | F | M | F | M | F | F | F | F | F |
| **Age (y)** | 79 | 75 | 82 | 76 | 80 | 81 | 82 | 83 | 75 |
| **Diagnosis** | AD | AD | AD | MCI | MCI | AD | AD | AD | AD |
| **Onset (y)** | 70 | 73 | 75 | 74 | 78 | 80 | 79 | 79 | 71 |
| **Dur (y)** | 9 | 2 | 7 | 2 | 2 | 1 | 3 | 4 | 5 |
| **Edu (y)** | 12 | 16 | 16 | 9 | 14 | 12 | 14 | 9 | 16 |
| **Medication** | Donepezil hydrochloride | Donepezil hydrochloride | Donepezil hydrochloride | Donepezil hydrochloride | Donepezil hydrochloride | Donepezil hydrochloride | Galantamine hydrobromide | Donepezil hydrochloride | Memantine hydrochloride |
| **Dosage** | 5 mg/QD | 5 mg/QD | 5 mg/QD | 10 mg/QD | 5 mg/QD | 5 mg/QD | 8 mg/BID | 5 mg/QD | 5 mg/BID |
| **Living with** | Daughter | Spouse | Spouse | Spouse | Spouse & Daughter | Spouse | Spouse | Daughters | Spouse |
| **Plays Tangram Puzzles with** | Daughter/ Grandson | Self | Self | Self | Self | Self | Self | Daughter/ Grandson | Self |
| **Entertainment** | Television | Walking | Television | Daily shopping, walking | Ballet | Walking/ Housework | Singing | Daily shopping/ walking/ housework | Taichi/Daily shopping/ Housework |
| **Alcohol Intake** | No | 360 mL/day * | No | No | No | No | No | No | 180 mL/day * |
| **Tobacco Use** | No | No | No | 10 cigarettes/ day | No | No | No | No | No |
| **Previous Career** | Office staff | Sales staff | Music teacher | Office staff | Office staff | Office staff | Housewife | Housewife | Housewife |
| **Retirement (y)** | - | 68 | 70 | 63 | 60 | 60 | - | - | - |

*: Japanese wine. Dur: duration; Edu: education; y: year; BID: twice a day; QD: once daily.

**Table 6.** Changes in scores over 180 days in Study 2.

| No. | Moca-J (S) | Moca-J (E) | MMSE (S) | MMSE (E) | TMT-B/A (S) | TMT-B/A (E) |
|---|---|---|---|---|---|---|
| 1 | 15 | 15 | 17 | 19 | 3.9 | 5.5 |
| 2 | 18 | 21 | 22 | 22 | 2.6 | 1.4 |
| 4 | 21 | 18 | 26 | 19 | 1.9 | 5 |
| 5 | 25 | 23 | 23 | 22 | 2.7 | 1.9 |
| 6 | 18 | 14 | 22 | 20 | 5.3 | 3.1 |
| 7 | 19 | 15 | 19 | 18 | 1.7 | 2.2 |
| 8 | 18 | 20 | 23 | 24 | 2.2 | 1.9 |
| 9 | 17 | 17 | 17 | 21 | 4.0 | 3.3 |
| 10 | 18 | 19 | 22 | 22 | 2.9 | 2.1 |

**Table 7.** Statistical analysis of cognitive outcomes based on MMSE and MoCA-J scores in nine participants after 180 days in Study 2.

| Total Score | Initial Day | Final Day | Z | *p* |
|---|---|---|---|---|
| MMSE | 21.2 ± 3.0 (17–26) | 20.8 ± 1.9 (18–24) | 0.300 | 0.764 |
| MoCA-J | 18.7 ± 2.8 (15–25) | 18.0 ± 3.0 (14–23) | 0.839 | 0.401 |
| TMT-B/A | 3.0 ± 1.6 (1.7–5.3) | 2.9 ± 1.4 (1.4–5.5) | 0.533 | 0.594 |

MMSE: Mini-Mental State Examination; MoCA-J: Japanese version of the Montreal Cognitive Assessment; TMT: Trail Making Test.

**Table 8.** Statistical analysis of cognitive outcomes based on MMSE scores in nine participants after 180 days in Study 2. Wilcoxon test.

| MMSE Score | Initial Day | Final Day | Z | *p* |
|---|---|---|---|---|
| Total | 21.2 ± 3.0 (17–26) | 20.8 ± 1.9 (18–24) | 0.300 | 0.764 |
| Orientation | 6.2 ± 1.9 (4–9) | 5.7 ± 1.6 (4–9) | 0.549 | 0.583 |
| Registration | 3.0 ± 0.0 (3) | 3.0 ± 0.0 (3) | 0.000 | 1.000 |
| Attention and calculation | 2.7 ± 1.9 (0–5) | 2.8 ± 1.8 (1–5) | 0.503 | 0.615 |
| Recall | 0.6 ± 0.7 (0–2) | 0.4 ± 0.5 (0–1) | 0.186 | 0.853 |
| Language and praxis | 8.8 ± 0.4 (8–9) | 8.9 ± 0.3 (8–9) | 1.000 | 0.317 |

MMSE: Mini-Mental State Examination.

## 4. Discussion

A previous study revealed that creative activities such as tangram puzzles might benefit patients with mild-to-moderate dementia after 6 weeks of training [21]. Study 1 showed significantly improved MMSE scores after tangram puzzle intervention in patients with early AD for 90 days, revealing that this game might help reverse the cognitive decline within a short time. Although the results were provocative, they should be interpreted with caution because this is an open-label, single-arm study with no control group. We cannot rule out the possibility that the observed improvement in MMSE scores occurred due to the retest effect. The retest effect, also known as practice effect, occurs in patients with dementia or healthy individuals when frequently evaluated via neuropsychological assessments. Gross et al. revealed that the retest effect in patients with dementia is nontrivial but is lower than that in healthy individuals [22]. Lee et al. used two alternate MMSE forms (with different contents but identical structures) and demonstrated that the retest effect was observed when the tests were conducted twice monthly (an increase in the mean MMSE score by 0.7 point); however, no statistical difference was observed between the two alternate form groups [23]. Furthermore, two studies have shown that MMSE remains reliable even when conducted repeatedly in patients with dementia. The mean MMSE total score in Study 1 increased by 3.9 points, which was promising, despite the retest effect.

As the duration of intervention in Study 1 was extremely short, we could not assess the effect of tangram puzzles on preventing the worsening of cognitive function in patients with early AD. Therefore, we performed Study 2, in which the intervention period was prolonged to 180 days. To minimize the retest effect, all neuropsychological assessments were performed only twice. The statistical results did not reveal a significant improvement in cognitive function measured using MMSE, MoCA-J, and TMT after 180 days of tangram puzzle intervention in patients with early AD or MCI. However, these results do not always indicate the lack of efficacy of tangram puzzles in assessing cognitive function. A previous study showed that patients with AD or MCI lost two points per year [22]. In another study, researchers recruited 87 patients with AD/MCI who were randomized to three groups: cognitive treatment (CT), physical activity treatment (PT), and control (CTRL) groups. The background information of patients with AD in the CTRL group (MMSE: 18.7 $\pm$ 2.3, age: 80 $\pm$ 7 years, appropriately prescribed) was similar to that in our Study 2 (MMSE: 21.2 $\pm$ 3.0, age: 79.2 $\pm$ 3.1 years, appropriately prescribed). This previous study revealed that the mean MMSE score decreased to approximately 15 after 6 months of observation without intervention, and the overall cognitive worsening occurred in CT and PT groups simultaneously but was lower than that in the CTRL group [24]. A meta-analysis demonstrated a decrease in MMSE score by 1.7 points after 18.6 weeks of observation without any intervention [25]. In contrast, the mean MMSE score in the present study decreased by only 0.4 points after 180 days. This difference revealed that cognitive training using tangram puzzles might have delayed the disease progression. Further studies using the randomized controlled trial design are warranted to determine whether tangram puzzles prevent cognitive decline in patients with early AD or MCI. Previous studies have revealed that older adults prefer slow-paced games [26,27], and serious games such as tangram puzzles would be appropriate for cognitive rehabilitation.

The present study has several limitations. This is an open-label, single-arm study without a control group; thus, we cannot draw definite conclusions. In particular, the effect of medication cannot be ruled out. Although we compared our data with the control group data from other studies, this is inadequate to draw a conclusion. To determine whether the observed trajectory of cognitive function should be attributed to tangram puzzles, the progression of cognitive function should be compared between two groups of patients—one group on medication only and another on medication and tangram puzzles. The number of participants was extremely small. The observation period was extremely short to examine the effect of cognitive intervention on the progression of neurocognitive disorders. Both studies were performed in a university hospital setting, and patients generally visit the

hospital with the expectation of achieving a better quality of life; thus, placebo effect may also contribute to the observed cognitive functions.

Notably, the patient populations were different between Study 1 and Study 2, which limits the simple comparison of these two studies. The mean age of participants in Study 1 was 66 years, with four participants working during the observation period. They had a strong desire to participate in the training and made some efforts with the expectation of achieving a better quality of life. Most of them received full support from family members/caregivers as they were still "young seniors"; thus, most of them followed instructions appropriately and solved Tangram puzzles at least 3 times weekly. The results revealed an increase in the mean MMSE score. In particular, orientation function showed a great improvement, which indicates better partial cognitive function after training. A previous study utilized a geometric puzzle task similar to the tangram task in this study and revealed that visuospatial functions are predominantly attributed to the right parietal lobe [28]. Another study demonstrated the dominance of the right hemisphere during the tangram task [14]; visuospatial skills could help individuals determine their orientation in space, indicating that the more frequently the tangram task training is performed, the better the visuospatial and orientation functions. This may explain why orientation improved in Study 1. The investigator did not measure attention specifically during the observation, but participants exhibited better attention when the study was completed.

The mean age of participants in Study 2 was 79 years, and they had been retired for >15 years. The cognitive function of these participants and their family members was barely expected to improve. Some participants could strictly follow the instructions. The investigator made extensive efforts to build trust and ensured clear and effective communication to encourage patient adherence [29,30]; however, the investigator noticed that patient adherence was driven by their needs. Improving and maintaining patient adherence is a great challenge if patients themselves do not account for their need to be treated.

Additionally, the observation period in Study 2 coincided with the COVID-19 pandemic. Isolation and quarantine caused high levels of stress among patients and caregivers, which might have worsened cognitive deficits [31–33].

Tangram puzzles could be generally recommended to patients with neurocognitive disorders because it is also an intergenerational game that allows grandparents to play with grandchildren without leaving their home, thus reducing the care burden, despite the weak evidence regarding the positive effect of tangram puzzles on cognitive function.

**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/psychiatryint4040036/s1. Figure S1. Instruction maps were printed on A3 paper. Figure S2. Instruction maps pamphlet. Figure S3. T1 target sample (Geometry image). Figure S4. T1 target sample (Number image). Figure S5. T2 target sample (Katakana image).

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** Research data are not shared. The raw data belonged to the present study cannot be made publicly available because the disclosure of personal data was not included in the research protocol of the present study. The data are not publicly available due to privacy and ethical restrictions.

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