Clinical Effects and Characteristics of Color, Number, and Word Content Elements in Computerized Training Programs for the Prevention of Cognitive Decline

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Research Article

Keywords: prevention, aging, degenerative brain disease, cognitive function, computerized training program

Posted Date: September 16th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-879998/v1

Abstract

Background: The biggest problem in an aging society is the development of degenerative brain disease in the elderly. Neurodegenerative brain disease can cause cognitive dysfunction and rapidly increase the prevalence of dementia and Parkinson's disease, posing a huge economic and social burden on the elderly. A computerized cognitive rehabilitation training system has been developed to prevent and train cognitive dysfunction, showing various clinical effects. However, few studies have analyzed components of contents such as memory and concentration training. In this study, the clinical effects and characteristics of the color, number and words elements were analyzed by subdividing the memory and concentration contents into elements, difficulty, and training methods.

Methods: Using a total of eight contents developed based on neuropsychology, 24 normal subjects with an average age of 60.58 ± 3.96 years were conducted 3 times a week, and training was received for 30 to 45 minutes per session. To determine the training effect, MMSE-K, an evaluation tool most closely related to cognitive therapy, was used. The number of errors and problem solving time used in the analysis were dataized by measuring the number of incorrect answers selected by the subject and the time spent solving the problem, respectively. Using t-test, the significance of different between before and after training was determined. Correlation between the number of errors and problem-solving time by week was determined using a trend line. All experimental procedures and evaluations were conducted after obtaining IRB approval from Dongguk University Ilsan Hospital (DUIH2020-07-001).

Results: The subjects' MMSE-K scores were 27.88 ± 1.70 points before intervention to 28.63 ± 1.69 points after three weeks of intervention. In each subdivided component, color element showed an effect of improving complex difficulty, number element had the most effective training effect, and word element had a predictive effect on cognitive decline.

Conclusions: A detailed analysis results of the components used in a computerized cognitive rehabilitation training system will help develop degenerative brain disease contents to be developed later, and is expected to contribute to a prevention-oriented medical paradigm

1. Background

Medical is a word with a broad meaning to improve people's quality of life, such as maintaining, recovering, and promoting health. The actual activity of medicine is called medical practice or medical action. The related technology has been recognized as medical technology. In the past, medical care had a strong perception of treating patients because they received medical treatment after symptoms appeared. For this reason, activities and technology development for treatment have progressed naturally. Advances in medical care have extended the lifespan of old persons and led the world's population to an aging society in conjunction with various causes such as a decrease in fertility rate and changes in global economy [1-3]. The increase in older persons has made it necessary for more financial support for medical activities. The time and amount used for treating them have exploded. According to social and economic necessity, various changes began to occur at the national level to optimize the cost of increasing medical expenses [4]. In other words, the perception of medicine began to change from treatment to prediction, prevention, and health management.

The biggest problem in an aging society is the occurrence of acquired abnormalities in the aging population. Older persons are at increasingly risk of diseases as the prevalence of various chronic diseases and brain diseases increases [5]. Among them, neurodegenerative brain disease imposes a huge economic and social burden on individuals because it requires high cost and long-term treatment [6-7]. If neurodegenerative brain disease progresses due to various causes, cognitive impairment can result from abnormal loss of function of the nervous system or certain brain regions. Cognitive impairment refers to memory impairment, concentration impairment, and deficits in perceptual function. The prevalence of dementia, Parkinson's disease, and depression is 5 to 10 times higher in patients with mild cognitive impairment than in general older persons [8-9].

As an index for predicting neurodegenerative brain disease, decline in cognitive function is evaluated [10]. Methods to evaluate cognitive function are divided into neurophysiology using bio-signals and neuropsychology using comprehensive paper tests. Among them, the neuropsychological method, which has each evaluation method by subdividing cognitive function, has been standardized. This method is recognized as a valid evaluation based on various research results[11-13]. As a method of training cognitive function, various system training methods are used. Among them, the RehaCom system and CoTras system, which use computerized cognitive rehabilitation training (CCRT) methods, are the most used computerized training system. CCRT-system is a training program developed with the goal of improving cognitive functions such as memory, attention, concentration, and perceptual ability using a computer [14-15]. Also, training programs that can be used at home through a mobile CCRT-system using portable devices are being developed. Various training contents for training programs are also being developed. Various studies have been conducted on clinical effects of these CCRT-system on cognitive improvement in patients with brain injury, stroke, and multiple sclerosis and in old persons [16-21].

However, although various studies exist to confirm the clinical training effect of the CCRT-system, there have been very few studies that subdivided the program into elements of color, number and word, difficulty, and training methods to confirm clinical features and effects. In this study, a total of eight contents for memory and concentration training that can be used in CCRT-system were developed. By subdividing the components of the developed CCRT system, the clinical effects and characteristics of the cognitive rehabilitation training effects of each element are presented. These components were subdivided into content elements, difficulty, correct answer selection method, problem presentation method, and training method.

The results of this study are expected to be helpful in the development of cognitive rehabilitation training contents that can be used in the CCRT-system and various mobile devices. It is also expected to reduce the prevalence of neurodegenerative brain disease due to aging. Finally, It provides a basis and contributes to a medical paradigm centered on prediction and prevention.

2. Methods

2-1 Contents design and setting

Contents used in this study were developed based on neuropsychology. Neuropsychology is a field that studies the relationship between brain regions and functions. Brain function is assessed using a variety of neuropsychology testing methods, including comprehensive intelligence, attention, memory, and language tests. The results are then analyzed to determine impairment of brain function. Accordingly, the developed contents were subdivided to enable cognitive rehabilitation training and brain health evaluation. It is expected that research results that can prevent and predict brain diseases can be obtained through these contents[22-23].

For the first time, we subdivided components that made up the contents of memory and concentration (Table 1). In order to specify the brain region, each element of these contents was subdivided into words, numbers, and color (Item 1 of Table 1). Words and language are recognized in Wernicke's area in the temporal lobe. The medial temporal lobe is responsible for declarative memory. The occipital lobe that is located in the visual cortex and ventral pathway connected to the temporal lobe processes and remembers color information while comparing existing color information with new color information. The parietal lobe connected to the dorsal pathway of the occipital lobe controls the integration of somatic sensory information such as touch, spatial function, and calculation to recognize numbers [24-26].

In difficulty, we included complexity to increase the number of errors (NOE) and problem solving time. A complication can be described as a kind of cluster. Contents with low difficulty are provided with clearly clustered words such as fruits and animals as a problem. Words that are not clustered are provided as those with higher difficulty. Also, the higher the difficulty, the greater the amount and length of the problems offered. As a result, the number of problems the subject must memorize and solve increases. (Item 2 of Table 1).

Next, the frontal lobe controls and processes information coming from other lobes, so the training method was subdivided in terms of information recognition and processing[27]. Because the subject should recognize and solve the problem of contents, the method of recognizing the problem (called RP-method) and the method of solving the problem (called SP-method) were subdivided. Sequential problem presentation method (sequential-RP), which sequentially shows problems one by one, and simultaneous problem presentation method (simultaneous-RP) for recognizing the problem by showing the problem at the same time, are used in the RP-method. In addition, the SP-method is divided into a sequential answer selection method (sequential-SP) in which correct answers are selected in the same order as the problem is presented and a random answer selection method (random-SP) in which correct answers are selected regardless of the order (Items 3 and 4 of Table 1). Finally, when selecting an incorrect answer, contents were developed by dividing the method of training repeatedly and the method of non-repetitive training (Item 5 of Table 1).

Table 1

Components and training methods by training contents

program	item 1	item 2	item 3	item 4	item 5
Contents	Element	difficulty	presentation method	selection method	training method
word memory	word	complication	sequential	random	repeat
number memory	number	length	simultaneous	sequential	repeat
color memory	color	length	sequential	sequential	repeat
word-picture memory	word-picture matching	length	sequential	random	repeat
word concentration	word	amount	simultaneous	random	non repeat
number concentration	number	mental arithmetic	simultaneous	sequential	non repeat
color concentration	word-color	amount	simultaneous	random	non repeat
scene concentration	scene	complication	simultaneous	random	non repeat

2-2 Content computerization design and setting

The word memory content sequentially shows a total of 5 random words from a cluster corresponding to fruit, animal, house, and landscape according to difficulty. Subjects remember a words and randomly clicked a button with the same word written on it (Fig. 1A). The number memory content shows a text with 2 to 6 numbers listed according to difficulty. Subjects remembered the number and clicked the numbered button in the order in which these numbers were listed (Fig. 1B). The color memory content sequentially shows images in which 1 to 5 colors are expressed according to difficulty. The subjects remembered the color and clicked the buttons of the same color in the order listed (Fig. 1C). The word-picture memory content sequentially shows 2-4 random words to the subject according to difficulty. Subjects remembered the presented words and randomly clicked a button with an image identical to the word (Fig. 1D).

The word concentration content must randomly select appropriate words from similar words such as N and M, T and Y. The amount of objects to be compared increases according to the difficulty (Fig. 1E). The number concentration content must select numbers in an ascending order. The size value of the object to be compared varies according to the difficulty. For example, rather than sequential values such as 1, 2, 3, non-sequential values such as 1, 4, 8 should be selected sequentially in an ascending order (Fig. 1F). For color concentration content, the correct answer is randomly selected by clicking the button whose background color. The written word color is the same (Fig. 1G). Finally, scene concentration content presents a specific scene to the subjects and the subjects randomly select an image that does not exist. The complication of images included in a scene increases with difficulty (Fig. 1H).

2-3 Study design and setting

The clinical evaluation design used in this study is shown in Figure 2. The evaluation was conducted after obtaining Institutional Review Board approval from Dongguk University Ilsan Hospital (DUIH2020-07-001). Since all subjects were trained with the same developed contents, the clinical study design was set up as a single group. In order to investigate the function and effect of contents, adult men and women over 55 years of age were designated as study subjects. Those with cognitive, physical, and behavioral disorders that would make it difficult to use the program were excluded through screening evaluation [28]. MMSE-K, an evaluation tool most closely related to cognitive rehabilitation training, was selected as an effectiveness evaluation tool to check the screening evaluation for subject recruitment and the training effect of the developed content. Training was conducted once a week for 30 to 45 minutes for 3 weeks. All processes were conducted with the investigator subjects to conduct training and provide assistance.

In the personal information survey, gender, educational background, medical history, and cognitive rehabilitation treatments were evaluated. Before proceeding with concentration and memory training, the orientation problem was preceded to familiarize basic movements and training methods. After orientation, concentration, and memory training, subjects filled out questionnaires on user satisfaction, time satisfaction, comprehension, and difficulty and the investigator evaluated the subject's training accuracy and training time.

2-4 Subject design and setting

Screening evaluation was conducted according to the study design. Cognitive training test results were obtained for 24 subjects, excluding 1 who dropped out (a total of 25 subjects) (Fig. 3). As a result of analyzing sex and age of subjects using the personal information survey, 7 (29.2%) males and 17 (70.8%) females of these 24 subjects participated. The average age of these 24 subjects was 60.58 ± 3.96 years old. Subjects received education at 16.7% college level (dropout or graduation), 50% high school level (dropout or graduation), 25%middle school level (dropout or graduation), and 8.3% others. As for medical history, 13 (54.1%) subjects had no medical history, 7 (29.2%) subjects had diabetes and hypertension, and 4 (16.7%) subjects had hyperlipidemia and esophagitis. There was no disease that could directly affect cognitive function in all subjects. However, diabetes, hypertension, and hyperlipidemia are classified as risk factors for brain disease. Thus, it is expected that the prevention effect can be confirmed according to the evaluation. Finally, 22 subjects (91.7%) had no experience in cognitive training and among those who experienced cognitive training, paper therapy and computer therapy were experienced by one each.

2-4 Data analysis design and setting

For the reliability of the evaluation paper used for the test subject, the Cronbach's alpha coefficient, the reliability coefficient of the respondent for various items at a fixed time, was used. The score of the evaluation paper was analyzed as average score, standard deviation, and percentage for items using a Likert scale. To record training accuracy and training time, the investigator recorded the number of incorrect answers selected by the subject and the training start and end times for each content during training.

All measured data were extracted by the investigator and recorded and entered into the data entry form. These extracted data were rearranged by week to observe the subject's changes in the weekly training process. Results values are presented as a percentage of the corresponding response/total response. T-test was used to compare data and confirm the significance of changes in incorrect answers and problem-solving time between before and after using cognitive training contents. The correlation between incorrect answers and time by week was determined using a trend line. After that, the correlation between incorrect answers and time was determined in weekly concentration and memory training. Clinical effects and characteristics were then determined according to subdivided parameters.

3. Results

3-1 MMSE-K evaluation

Before the subdivided parameter analysis of contents, MMSE-K values before and after training were compared to check the effect of actual training. On the MMSE-K, the range of cognitive scores for normal individuals is usually 24-30. The subject's MMSE-K score increased to 27.88 ± 1.70 before the developed content training and 28.63 ± 1.69 after 3 weeks of training. Therefore, it was confirmed that the developed 8 contents had cognitive rehabilitation effects even within the normal cognitive range (Table 2).

Table 2

Changes in MMSE-K values before and after the training program

Subjects (n = 24)				
MMSE-K	pre	post	Difference Mean ± SD	p-value
	27.88 ± 1.70	28.63 ± 1.69	0.75 ± 2.42	0.142

3-2 Satisfaction evaluation

Evaluation scores of subjects' program satisfaction survey questionnaires were analyzed (Table 3). The maximum score per item is 20 points. User satisfaction, time satisfaction, comprehension, and difficulty of evaluation items mean how to use and its convenience, preparation time and correct answer selection time, problem interpretation such as words and pictures, and difficulty according to time, respectively. In the evaluation, scores were decreased for all items corresponding to memory training. This means that the training method in which the problem is repeated when selecting the wrong answer according to item 5 of Table 1 can greatly reduce the satisfaction of contents.

Table 3

Program satisfaction survey questionnaire evaluation score

by week	User Satisfaction		time Satisfaction		understanding		difficulty	
	concentration	memory	concentration	memory	concentration	memory	concentration	memory
1 week	16.17	18.33	15.29	16.88	15.63	17.17	15.17	17.17
2 week	15.46	16.88	15.68	16.13	16.04	16.38	16.00	16.83
3 week	17.08	17.00	16.46	15.42	17.67	16.42	17.17	15.67
Mean score	16.236	17.40	15.81	16.14	16.44	16.65	16.11	16.55
changed score	0.91	-1.33	1.17	-1.46	2.04	-0.75	2	-1.5

3-3 Effective contents training time

Next, the relationship between NOE and solving time by week of all training was analyzed. As a result of the t-test, the NOE and solving time in 1 week were 0.60±1.08 NOE, 31±17.05 seconds, comparison values in 2 week were 0.49±0.74 NOE, and 29.58±17.51 seconds, indicating $P>0.05$. However, the comparative values in 3 week were 0.35±0.51 NOE, and 24.72±12.13 seconds showed $P<0.05$, so in order to obtain the effectiveness of training clearly, at least 3 weeks of training time should be taken. In addition, by analyzing the trend line displayed according to the number of errors in week 1 and week 3, it was confirmed that effective training is possible when the configuration time for each difficulty is within 45 seconds(fig 4 B).

3-4 Difference according to how to choose a problem

The NOE and problem solving time relationship was analyzed by dividing concentration and memory contents. However, because we could not find any clear difference in concentration or memory content, we reclassified data according to item 4 in Table 1 to analyze the relationship between NOE and problem solving time(Fig. 5). It had different characteristics that compared A) in Fig. 5, which used random-SP, and B) in Fig. 5, which used sequential-SP. Accordingly, in order to confirm the training effect by week, the content was rearranged as a weekly error time graph and shown as C) and D) in Fig. 5.

As a result of the analysis of how to choose the problem, the following training effects were demonstrated. training contents using random-SP shortened the problem-solving time after the weekly training while training contents using sequential-SP reduced incorrect answer rate for the same time zone after the weekly training.

3-5 Difference according to how to present a problem

In addition to the method of selecting the correct answer in training, the method of presenting the problem is also a component (Table 1, item 3). For the first time, we compared contents using different problem presentation methods among contents using random-SP (Fig.

6). As shown in results of 3-4 above, random-SP shows the tendency of training effect to reduce the problem solving time. However, in the content using sequential-RP (Fig. 6C, 6D), the decrease width in problem-solving time receded compared to other content, while the NOE showed a tendency to increase.

Additionally, among contents using sequential-SP, contents using different problem presentation methods were compared (Fig. 7). Sequential-SP Shows the trend of the training effect to reduce the number of incorrect answers. Unlike other contents using simultaneous-RP, when sequential-RP was used (Fig. 7 A), the NOE and solving time increased at 2 weeks. According to these results, sequential-RP of RP-method in development of content had a greater influence on subjects than SP-method, which might have induced an increase in NOE in the training process.

3-6 Training effect by element and difficulty

Elements were compared based on contents with the most similar components. Figure 8 shows the training effect for each week according to the difficulty setting of word, number, and color element used in content. It was confirmed that the NOE and problem-solving time gradually increased according to the complexity and length of the difficulty. When the initial difficulty and the final difficulty were compared by week, the average number of errors and problem-solving time increased by 0.14 NOE and 12.74 seconds in word memory, 0.31 NOE and 8.03 seconds in number memory, and 1.89 NOE and 31.42 seconds in color memory.

Next, the total NOE and problem-solving time by week were compared. In the 1 week and 3 week of the word memory, there was no change in the average error rate from 0.05 to 0.05 NOE, while the average problem-solving time decreased from 32.21 to 29.82 seconds. In number memory content, average error rate decreased from 0.23 to 0.14 NOE and average problem-solving time decreased from 18.85 to 15.39 seconds. In color memory content, average error rate decreased from 0.80 to 0.74 NOE and average problem-solving time decreased from 25.00 to 22.00 seconds.

In addition, as shown in Figure 9, in the word concentration and number concentration contents using the difficulty of amount and mental arithmetic, the NOE and solving time were increased while weekly. In the word concentration, average NOE and solving time for word concentration decreased from 0.30 to 0.21 NOE and from 36.34 to 28.19 seconds and in the number concentration, average error rate decreased from 3.58 to 1.83 NOE and average problem solving time decreased from 36.34 to 28.17 seconds.

Through these results, several characteristics could be confirmed. First, difficulty such as complication, length, amount, and mental arithmetic used in content development can increases the processing process and time of problem solving. Second, the incorrect answer rate for each element was high in the order of color, number, and word and the solving time was higher in the order of color, word, and number. Accordingly, content including color element may be classified as high difficulty. Third, the number element had the slightest solving time and the highest weekly incorrect answer reduction rate (Fig. 8C, Fig. 9C). Contents including numeric elements were judged to be effective as short-term training. Finally, it was confirmed that incorrect answer rate of word memory using word element was significantly lower than that of other elements. It was judged that the current test subjects had little difficulty in recognizing words.

4. Conclusions

The increase in medical expenses, which is a side effect of the aging society caused by the increase in the aging population, has provided us an opportunity to change from a treatment-oriented medical paradigm to a prevention-oriented medical paradigm that can manage patients and older persons at a much lower cost than treatment costs. Accordingly, various countries are making efforts to prevent and predict degenerative brain diseases known to have a high economic and social burden. Degenerative brain disease is known to be caused by genetic and environmental problems and neurodegeneration that can damage normal cells with aging, thus greatly increasing the prevalence of various degenerative brain diseases such as Alzheimer's, Parkinson's, and multiple sclerosis [29]. Degenerative brain disease causes cognitive impairment, a neurological complication that impairs intellectual functions such as memory, concentration, judgment, and language skills. Cognitive impairment can cause various deficits in neuropsychological function in the initial mild state, eventually leading to severe cognitive impairment [30]. In this study, a total of 8 training contents were developed based on neuropsychology to prevent cognitive decline. Their clinical effects and changes were derived by subdividing components to classify brain regions.

Through MMSE-K, the cognitive rehabilitation training effect of a total of 8 training contents was confirmed. As a cognitive function test, the MMSE-K, revised according to the characteristics of Korean society, has been proven the validity of attention, computational power, language, memory registration and memory recall, and visual composition evaluation methods[31]. In this study, through training conducted on 24 subjects aged 60.58 ± 3.96 years for 3 weeks, the initial score was 27.88 ± 1.70. It was changed to 28.63 ± 1.69, showing an increase of 0.75 ± 2.42. In previous studies, cognitive rehabilitation and control training were conducted for about 9 weeks for 15.95 ± 6.46 subjects with an average age of 73.70 ± 3.72 years. The initial subject's MMSE score was 22.19 ± 2.5. However, the difference in MMSE after training was 0.10, which showed an insignificant training effect [32]. In other words, it is judged that the computerized training program proposed in this study to prevent cognitive decline will have a greater expected effect if it is used for the normal elderly population rather than for the mild patient group. Based on these results, the computerized cognitive rehabilitation training programis expected to be used as a method to prevent aging and functional deterioration of cranial nerves, rather than treating already damaged cranial nerves [33].

The main purpose of segmented contents is to represent regions of the brain. The brain has one large mass of cells. The brain maintains various physical coordination and homeostasis. It is responsible for functions necessary for life activities. It is also responsible for cognition, emotion, memory, and learning. The brain is largely divided into three parts: cerebrum, cerebellum, and brainstem. The cerebrum is the center of mental activity. The outer layer of the cerebrum is composed of four lobes. In this study, language, number, color, and training method were designated as the temporal lobe, parietal lobe, occipital lobe, and frontal lobe, respectively. Accordingly, this study focused on brain atrophy and functional decline that would occur during natural aging [34]. Atrophy, the most common aging process in the brain, represents morphological changes due to a decrease in brain volume. It is very difficult to find atrophic patterns in the brain. However, brain atrophy can be predicted based on a decrease in various functions responsible for specific brain regions[35].

The developed content included each element with words, numbers, and colors. The error rate increased in the order of words, numbers, and colors according to training results. These results were expected to have a specific relationship in the temporal lobe, parietal lobe, and occipital lobe through segmentation of brain regions. The local gyrification index, which determines cortical complexity, is known to be a potential factor for predicting cognitive decline due to brain atrophy. In this study, the local gyrification index corresponding to each brain region was analyzed. According to previous research papers, the local gyrification index is low in the order of the temporal lobe, parietal lobe, and occipital lobe. In addition, the local gyrification index of the occipital lobe is 22% lower than that of the temporal lobe. For this reason, the order of error rate is listed. It was judged that higher error rates occurred in color elements than in word and number elements. Additionally, number concentration and memory content showed greater training effect than other trainings [36]. That is, it is expected that nerve activation according to stimulation occurred significantly in a state in which functions such as memorizing and calculating numbers were deteriorated.

Based on the relationship between the subdivided element and the local gyrification index, it was confirmed that the element used for the content directly or indirectly reflected and affected the brain region. This study proposed the following final effects and characteristics according to elements. Color recognition and memory in the occipital lobe, which has a low basic local gyrification index, might be difficult. However, since the occipital lobe has the temporal lobe in charge of words and the parietal lobe in charge of numbers with pathways, it seems that the color element can be used in combination with one additional element. In other words, it will be possible to develop and utilize more difficult training contents. The number element is judged to be the most effective training element to be performed in older persons. With aging, the existing functions and new learning functions of the parietal lobe are decreased compared to those in young adults. These functions show a decrease in subjective experience [37]. Words and color elements are in the form of presenting what they already know. However, numbers can suggest a variety of new problems through new combinations and calculations. It was determined that existing known calculations and recognition methods could be utilized.

Finally, it is expected that word elements can be used as a prediction of cognitive decline. The brain regions responsible for memory include the medial temporal lobe, the frontal lobe, and the hippocampus. In this study, the role of the medial lateral lobe was emphasized. The reason is that the medial temporal lobe is not the ultimate storage location for memories, it is a temporary storage location[38]. That is, it was determined that the role of the medial temporal lobe would be large because word memory is a content that solves problems using temporary memory. In word memory contents using words, the change in incorrect answer rate was insignificant compared to other contents. For this reason, it is presumed that word learning using nameable objects observed and used in daily life can stimulate the medial temporal lobe and affect the memory process and the processing of memory processes in the brain, suggesting that they are functioning normally at the normal age of 60.58 ± 3.96 years. Finally, based on results of various studies in which the function and volume of the medial temporal lobe are decreased in those with mild cognitive disorders such as Alzheimer's disease [42-44], the occurrence and change of a large error rate of content using word element can to be utilized as a predictor of degenerative brain disease.

Although there was a slight difference depending on the factors, the training effect also differed according to the method of choosing the correct answer and the method of presenting the problem. In this study, it was assumed that these training methods were related to the prefrontal area. The frontal lobe regulates brain functions. It is an area involved in complex cognitive function-related processes such as solving new problems. Also, the frontal lobe is associated with the memory of events and temporal sequences [45]. In this study, events were set as a method of presenting problems at the same time and the temporal order was set as a method of presenting sequential problems. In this study, the method of presenting sequential problems produced more errors. The method of presenting sequential problems was judged to be related to the network function of the frontal lobe and it was confirmed through various studies.

A study on frontal lobe injury has been confirmed that actual frontal lobe injury patients can perform routine memory tests normally [46]. However, it was confirmed that there was a disability in the study focusing on the strategic process test using tactical aspects such as the memory of temporal sequence [47-48]. Results of previous studies and the present study confirmed that the problem presentation method was related to the frontal lobe. It was judged that the strategic process function of subjects who were 60.58 ± 3.96 years old was somewhat weakened. Finally, training using the sequential problem presentation method for frontal lobe activation requires at least three weeks of training time and training using color elements can create a greater effect (Fig. 7A).

Existing training and evaluation have used paper equipment. However, this study performed a computerized training program using computers. Accordingly, the effect of using a computer and training device was additionally confirmed. As older people lose concentration and increase fatigue due to aging, the training time of the content used for training should be taken into account. The gradual increase in the training effect by week and the sharp increase in the incorrect answer rate in the 3rd week decreased. That is, in training using a computer and training device, a solution time of 45 seconds or more may cause a decrease in concentration and an increase in fatigue. In addition, through the satisfaction survey, it was found that repeated training had an additional effect on incorrect answers and concentration or fatigue since repeated training could decrease test subject's training satisfaction when an incorrect answer was selected.

However, this study has some limitations. First, the period of training was short. In a previous study, the cognitive rehabilitation training and adjustment period lasted an average of 9 weeks. Accordingly, final results were presented when training and adjustment were carried out and changes were completed. In this study, although the effect and specificity of training were suggested, the final change was not quantified numerically. In addition, as shown in FIGS. 6C and 6D , a reduction effect after the increased error rate was not confirmed. Nevertheless, compared to the previous study, subjects who were younger than the previous study participated in this study. Results confirmed that cognitive function could be improved by 3 weeks of training for subjects with normal cognitive function, thereby preventing cognitive decline. Second, the condition of the subject could not be maintained the same. The effect of training is expected to vary depending on concentration and fatigue. However, in this study, physical or bio-signal data measurements other than verbal confirmation could not be used to check the condition of these subjects. Thus, the analysis was carried out by removing the occurrence of serious errors through the process of Figure 4.

In summary, this study analyzed clinical effects and characteristics of content elements that could help develop a computerized instructional program for preventing cognitive decline in line with the prevention and prediction-centered medical paradigm. Through this study, it is expected that customized content production will be possible using elements and training methods suitable for each characteristic in the program used for degenerative brain disease prevention contents and devices developed in a variety of ways. It is expected to be helpful in clinical research and planning. Results of this study are expected to contribute to the development of a computerized cognitive rehabilitation training program that can predict and prevent degenerative brain diseases occurring in a rapidly changing aging society, thereby contributing to a prevention-oriented medical paradigm.

Abbreviations

CCRT : computerized cognitive rehabilitation training; NOE : the number of errors; RP-method : the method of recognizing the problem; SP-method : the method of solving the problem; sequential-RP : sequential problem presentation method simultaneous-RP : simultaneous problem presentation method; sequential-SP : sequential answer selection method; random-SP : random answer selection method

Declarations

Ethics approval and consent to participate

The study was conducted according to the principles of the Declaration of Helsinki. This study was approved by the Institutional Review Board of Dongguk University Ilsan Hospital with the Protocol Number DUIH2020-07-001. Participants read and signed an informed written consent form before participating in the study. It is not possible to identify the patient using the data in this study.

Consent for publication

Not applicable.

Availability of data and material

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Competing interests

The authors have no conflict of interest to report.

Funding

This work was supported by the Technology Innovation program – Advanced Technology Center (ATC) 10076733, “Development of the cognitive rehabilitation solution for patients with cognitive impairment using speech recognition and eye tracking technology”, funded by the Ministry of Trade, Industry & Energy (MOTIE, Korea)

Authors' contributions

DCK, JHJ devised this study. DCK analyzed the basic elements of cognitive rehabilitation training content and developed it using Android Studio in the form of CCRT. In addition, analysis and interpretation of the result values were carried out. JHJ and SMK set up the clinical procedure. The clinical procedure should be able to confirm the clear effect of the training effect and should be able to reflect the characteristics of the CCRT system well. Accordingly, the final research procedure was decided through a meeting with the IRB of Dongguk University and reflection of opinions. NHK and YJL participated in all evaluations as investigators, helped the subjects in the training process, and wrote incorrect answers and time.

Acknowledgements

This study is funded by the Ministry of Trade, Industry & Energy (MOTIE, Korea). We gratefully acknowledge the Ministry of Trade, Industry & Energy.

References

1. Ogura, Seiritsu, and Mihajlo Michael Jakovljevic. "Global population aging-health care, social and economic consequences." Frontiers in public health 6 (2018): 335.
2. Bloom, David E., David Canning, and Alyssa Lubet. "Global population aging: Facts, challenges, solutions & perspectives." Daedalus 144.2 (2015): 80–92.
3. OECD. Pensions at a Glance 2013: Retirement-Income Systems in OECD and G20 Countries [Internet]. Paris: OECD; 2013. Available: http://www.oecd.org/pensions/pensionsataglance.htm
4. Cristea, Mirela, et al. "The impact of population aging and public health support on EU labor markets." International journal of environmental research and public health 17.4 (2020): 1439.
5. World Health Organizacion. WHO. Envejecimiento y ciclo de vida [Internet]. 2018.[cited 2018 Jan 21]. Available from: http://www.who.int/ageing/about/facts/es/

6. Kim, Yoo Sung, and Bo-Eun Yoon. "Altered GABAergic signaling in brain disease at various stages of life." Experimental neurobiology 26.3 (2017): 122.
7. DiLuca, Monica, and Jes Olesen. "The cost of brain diseases: a burden or a challenge?." Neuron 82.6 (2014): 1205–1208.
8. Madero, Magdalena, Ambreen Gul, and Mark J. Sarnak. "Cognitive function in chronic kidney disease." Seminars in dialysis. Vol. 21. No. 1. Oxford, UK: Blackwell Publishing Ltd, 2008.
9. Petersen RC, Doody R, Kurz A, Mohs RC, Morris JC, Rabins PV, Ritchie K, Rossor M, Thal L, Winblad B: Current concepts in mild cognitive impairment. Arch Neurol 58: 1985– 1992, 2001
10. Eun Hyun Seo, PhD. "Neuropsychological Assessment of Dementia and Cognitive Disorders." Journal of Korean Neuropsychiatric Association 57.1 (2018): 2–11.
11. McCarthy, Rosaleen A., and Elizabeth K. Warrington. "Cognitive neuropsychology: A clinical introduction." (1990).
12. Folstein MF, Folstein SE, McHugh PR: “Mini-mental state” A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12:189–198, 1975
13. Meyer J, Xu G, Thornby J, Chowdhury M, Quach M: Longitudinal analysis of abnormal domains comprising mild cognitive impairment (MCI) during aging. J Neurol Sci 201:19–25, 2002
14. Rego, Paula, Pedro Miguel Moreira, and Luis Paulo Reis. "Serious games for rehabilitation: A survey and a classification towards a taxonomy." 5th Iberian conference on information systems and technologies. IEEE, 2010.
15. Huang, Jia, et al. "Effects of acupuncture and computer-assisted cognitive training for post-stroke attention deficits: study protocol for a randomized controlled trial." Trials 16.1 (2015): 1–10.
16. Fernández, Elízabeth, et al. "Clinical impact of RehaCom software for cognitive rehabilitation of patients with acquired brain injury." MEDICC review 14.4 (2012): 32–35.
17. Pantzartzidou, Alexandra, et al. "Rehacom software application is effective in cognitive rehabilitation of patients with brain injuries." Physical Medicine and Rehabilitation Research 2.1 (2017): 1–4.
18. Yang, Shanli, et al. "The synergistic effect of acupuncture and computer-based cognitive training on post-stroke cognitive dysfunction: a study protocol for a randomized controlled trial of 2× 2 factorial design." BMC complementary and alternative medicine 14.1 (2014): 1–11.
19. Barbosa, Hugo, António V. Castro, and Eurico Carrapatoso. "Serious games and rehabilitation for elderly adults." GSJ 6.1 (2018): 275.
20. Amiri, Sanaz, et al. "Effect of RehaCom cognitive rehabilitation software on working memory and processing speed in chronic ischemic stroke patients." Assistive Technology just-accepted (2021).
21. Cerasa, Antonio, et al. "Computer-assisted cognitive rehabilitation of attention deficits for multiple sclerosis: a randomized trial with fMRI correlates." Neurorehabilitation and neural repair 27.4 (2013): 284–295.
22. Casaletto, Kaitlin B., and Robert K. Heaton. "Neuropsychological assessment: Past and future." Journal of the International Neuropsychological Society: JINS 23.9–10 (2017): 778.
23. Kwak, Seyul, et al. "Distributed functional connectivity predicts neuropsychological test performance among older adults." Human Brain Mapping (2021).
24. Fonseca, Agnes Trebuchon-Da, et al. "Brain regions underlying word finding difficulties in temporal lobe epilepsy." Brain 132.10 (2009): 2772–2784.
25. Ueno, Aya, et al. "Reactivation of medial temporal lobe and occipital lobe during the retrieval of color information: A positron emission tomography study." Neuroimage 34.3 (2007): 1292–1298.
26. Cohen, Laurent, et al. "Language and calculation within the parietal lobe: a combined cognitive, anatomical and fMRI study." Neuropsychologia 38.10 (2000): 1426–1440.
27. Choi, Tae Jin, et al. "Determination of the concentrated state using multiple EEG channels." International Journal of Computer, Electrical, Automation, Control and Information Engineering 8.8 (2014): 1373–1376.
28. Sang-Hwan Kim, et al. "Cognitive Function and Dementia-related Risk Factors in Elders above 50 Years Old " Korean Journal of Clinical Geriatrics 6.2 (2005): 217–224.
29. McGEER, PATRICK L., and EDITH G. McGEER. "Inflammation and the degenerative diseases of aging." Annals of the New York Academy of Sciences 1035.1 (2004): 104–116.

30. Mitchell, Alex J., et al. "The influence of cognitive impairment on health-related quality of life in neurological disease." Acta Neuropsychiatrica 22.1 (2010): 2–13.
31. Kang, Yeonwook, Duk L. Na, and Seunghae Hahn. "A validity study on the Korean Mini-Mental State Examination (K-MMSE) in dementia patients." Journal of the Korean neurological association 15.2 (1997): 300–308.
32. Clare, Linda, and Bob Woods. "Cognitive rehabilitation and cognitive training for early-stage Alzheimer's disease and vascular dementia." Cochrane database of systematic reviews 4 (2003).
33. Chapman, Sandra B., et al. "Neural mechanisms of brain plasticity with complex cognitive training in healthy seniors." Cerebral cortex 25.2 (2015): 396–405.
34. Takeda, Shumpei, and Taiju Matsuzawa. "Brain atrophy during aging: a quantitative study using computed tomography." Journal of the American Geriatrics Society 32.7 (1984): 520–524.
35. Grajauskas, Lukas A., et al. "MRI-based evaluation of structural degeneration in the ageing brain: Pathophysiology and assessment." Ageing research reviews 49 (2019): 67–82.
36. Dajeong Kim, “Changes in human cortical gyral complexity pattern during normal aging: Analysis of cortical gyrification index.” Seoul National University Graduate school, 2012.
37. Ally, Brandon A., et al. "Parietal contributions to recollection: Electrophysiological evidence from aging and patients with parietal lesions." Neuropsychologia 46.7 (2008): 1800–1812.
38. Squire, Larry R. "Memory and brain systems: 1969–2009." Journal of Neuroscience 29.41 (2009): 12711–12716.
39. Smith, Michael E., June M. Stapleton, and Eric Halgren. "Human medial temporal lobe potentials evoked in memory and language tasks." Electroencephalography and clinical neurophysiology 63.2 (1986): 145–159.
40. Nobre, Anna C., and Gregory McCarthy. "Language-related field potentials in the anterior-medial temporal lobe: II. Effects of word type and semantic priming." Journal of neuroscience 15.2 (1995): 1090–1098.
41. Halgren, Eric, et al. "Processing stages underlying word recognition in the anteroventral temporal lobe." Neuroimage 30.4 (2006): 1401–1413.
42. Parra, Mario A., et al. "Medial temporal lobe function during emotional memory in early Alzheimer’s disease, mild cognitive impairment and healthy ageing: an fMRI study." BMC psychiatry 13.1 (2013): 1–12.
43. Chan, Dennis, et al. "Patterns of temporal lobe atrophy in semantic dementia and Alzheimer's disease." Annals of neurology 49.4 (2001): 433–442.
44. Visser, P. J., et al. "Medial temporal lobe atrophy predicts Alzheimer's disease in patients with minor cognitive impairment." Journal of Neurology, Neurosurgery & Psychiatry 72.4 (2002): 491–497.
45. Romine, Cassandra Burns, and Cecil R. Reynolds. "Sequential memory: a developmental perspective on its relation to frontal lobe functioning." Neuropsychology review 14.1 (2004): 43–64.
46. Janowsky, Jeri S., Arthur P. Shimamura, and Larry R. Squire. "Source memory impairment in patients with frontal lobe lesions." Neuropsychologia 27.8 (1989): 1043–1056.
47. Centeno, M., et al. "Memory in frontal lobe epilepsy." Epilepsy research 91.2-3 (2010): 123–132.
48. Shimamura, Arthur P., Jeri S. Janowsky, and Larry R. Squire. "Memory for the temporal order of events in patients with frontal lobe lesions and amnesic patients." Neuropsychologia 28.8 (1990): 803–813.

Figures

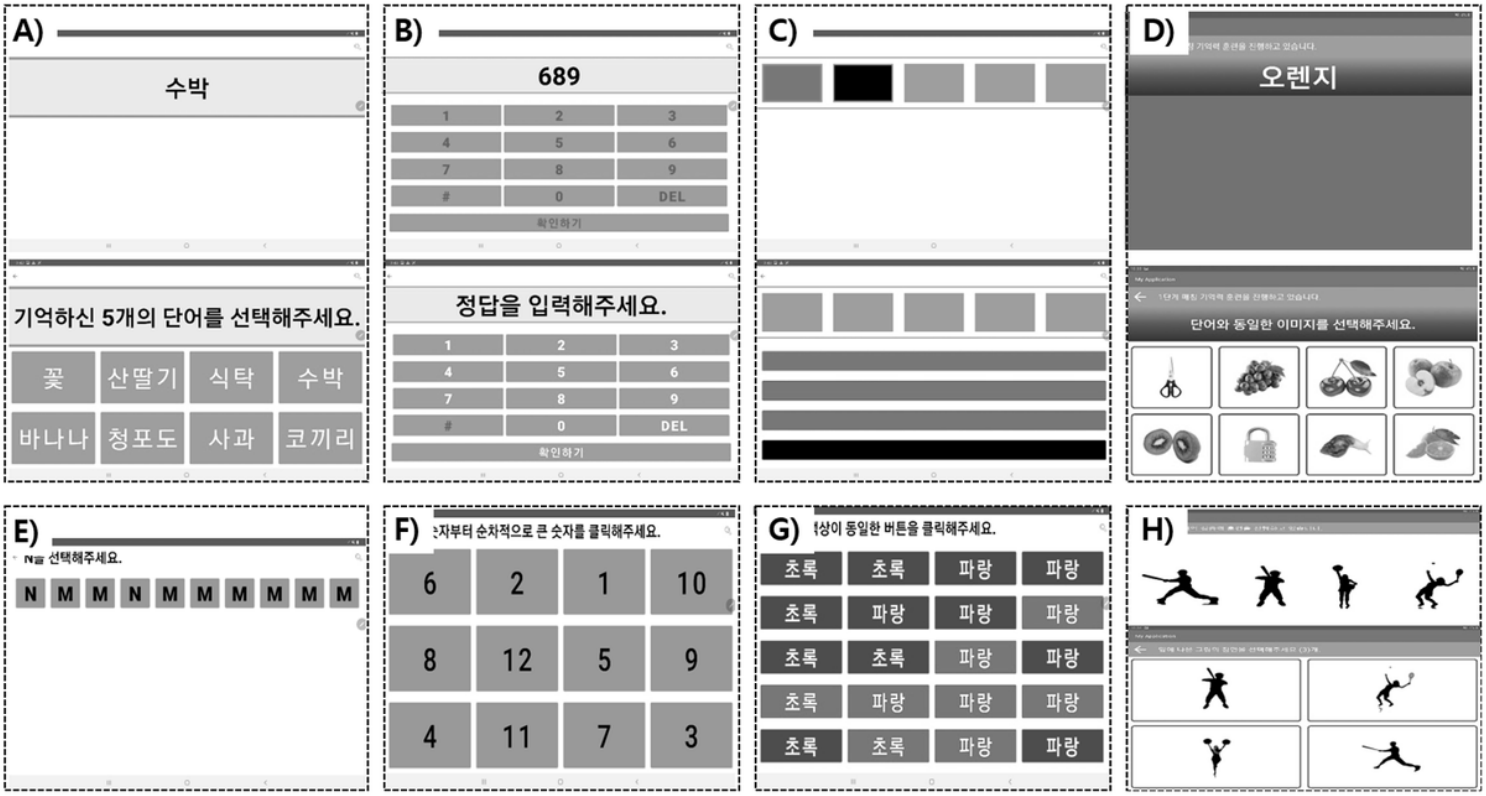

Figure 1

Developed Memory and concentration contents: A) Word memory, B) Number memory, C) Color memory, D) Word-picture memory, E) Word concentration, F) Number concentration, G) Color concentration, H) Scene concentration.

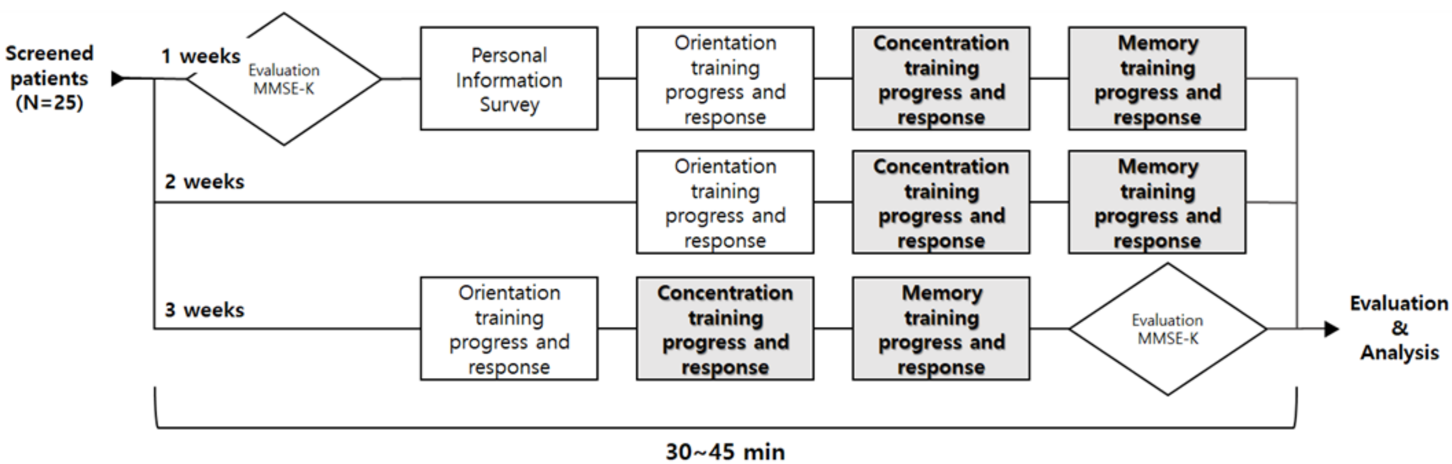

Figure 2

Study design for training program evaluation.

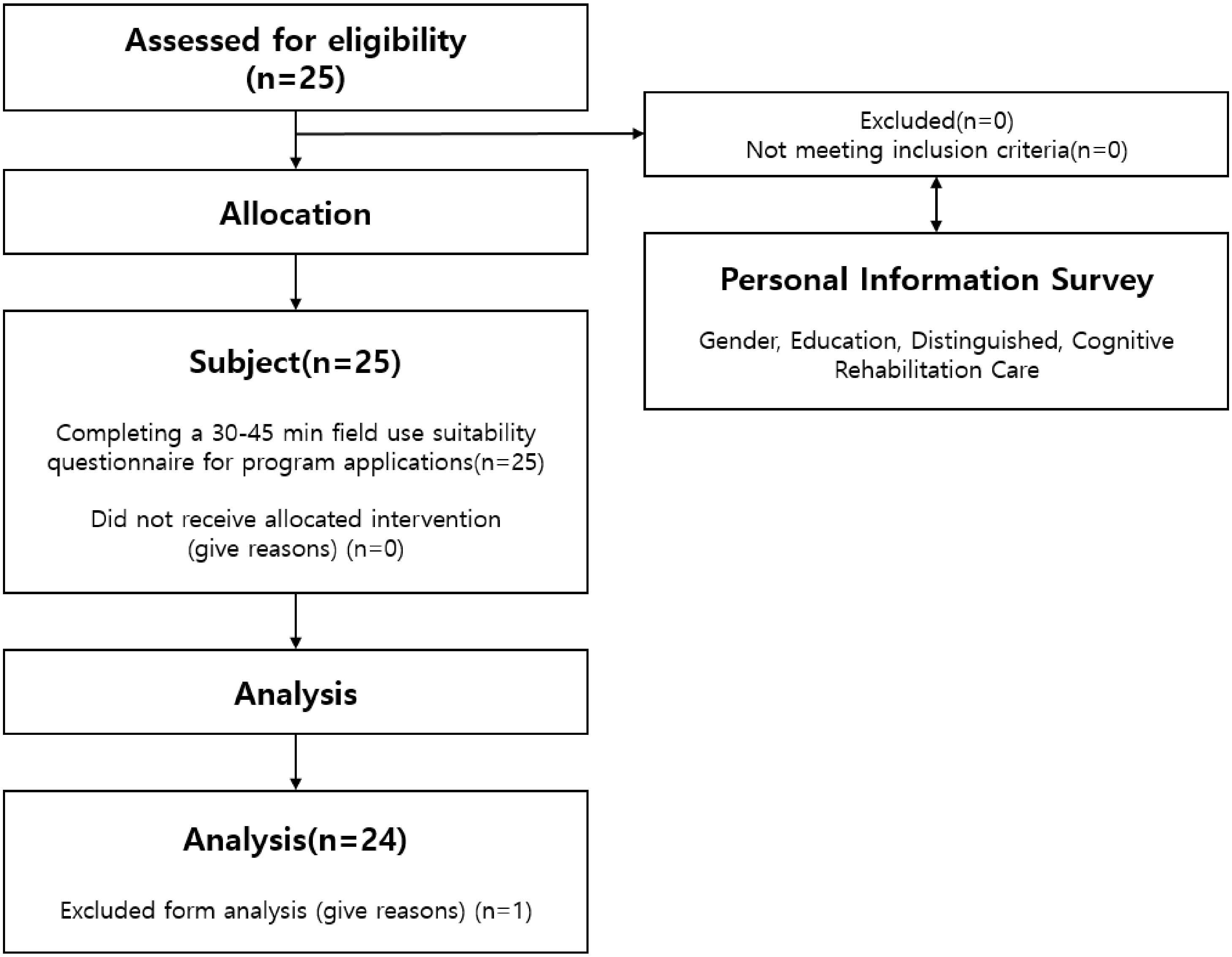

Figure 3

Screening evaluation and results for subject recruitment.

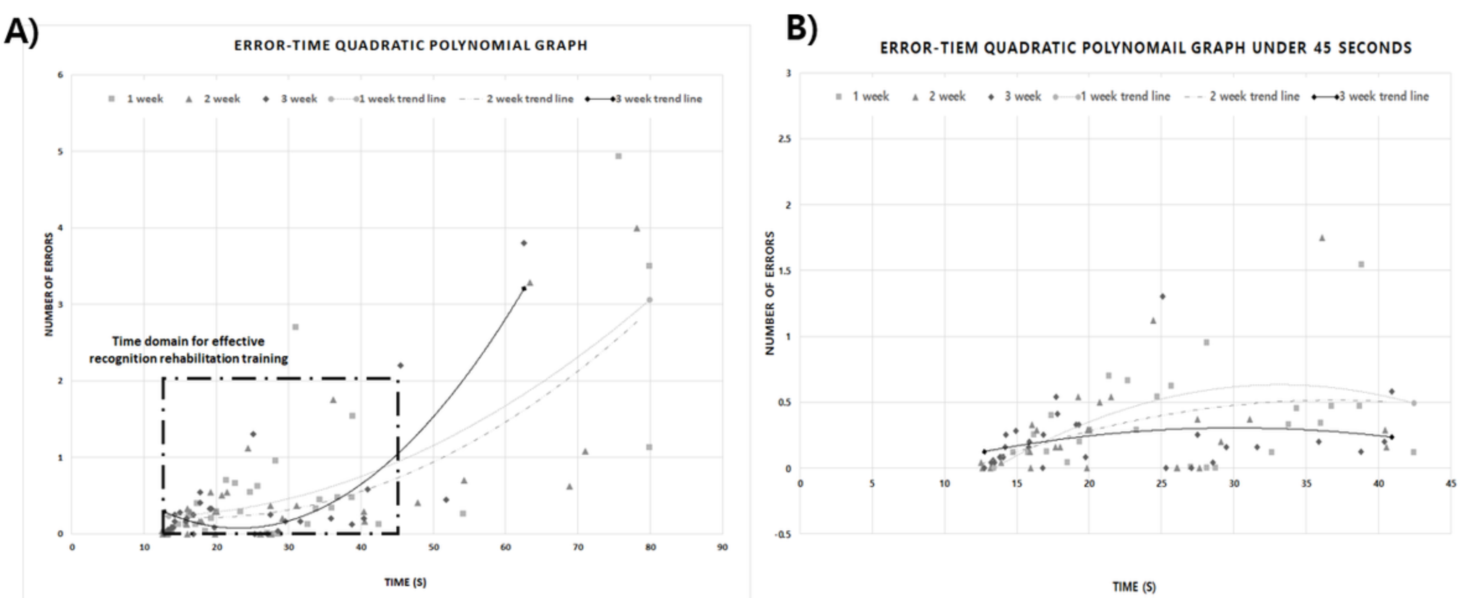

Figure 4

Scatter plot and quadratic polynomial trendline for error-time relationship analysis, A) graph includes all training time and number of errors, B) In the graph, the time for the number of errors in the 3 week to reverse the number of errors in the 1 week was calculated. After that, errors that has time longer than 45 seconds was removed and rearranged.

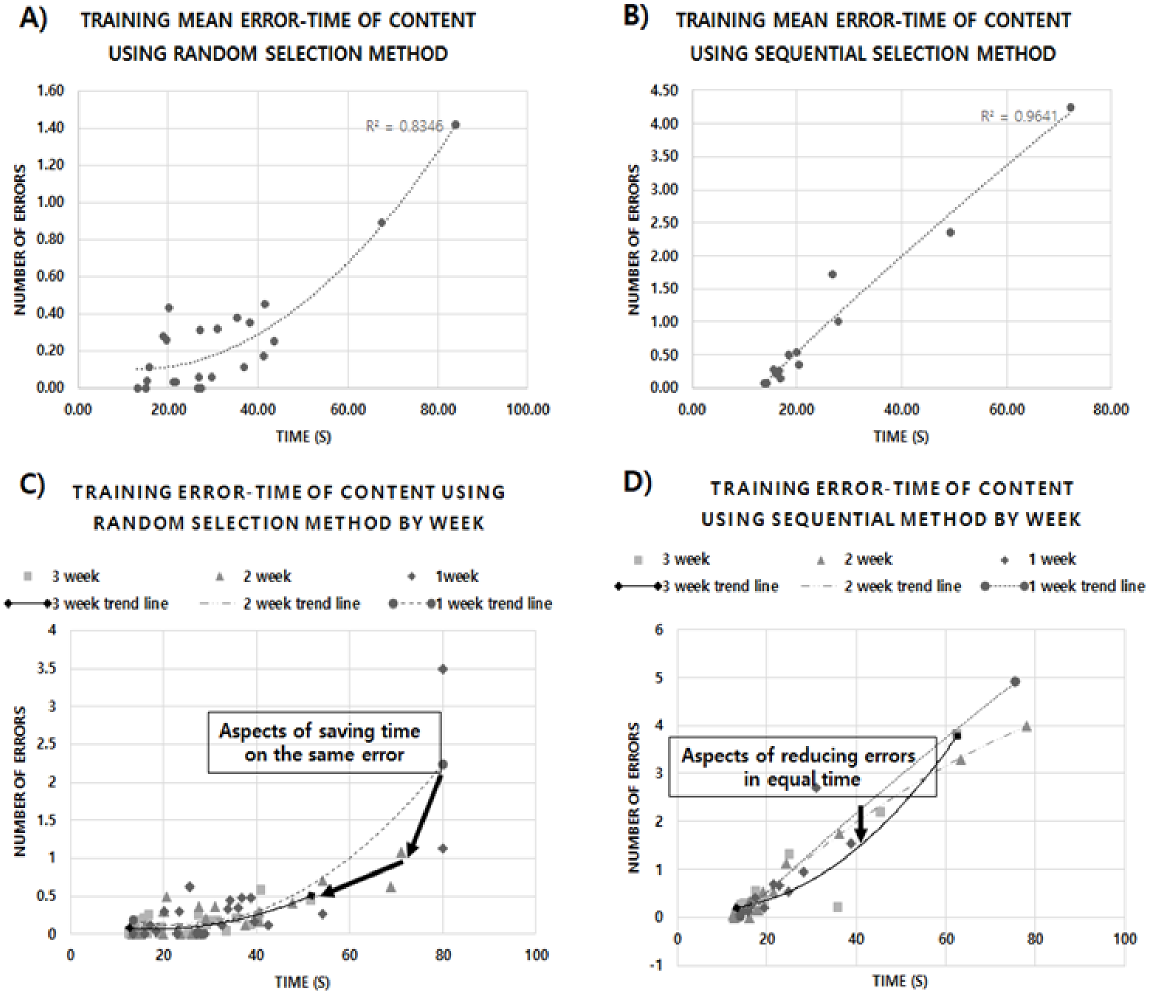

Figure 5

Difference according to how to choose a problem. A) Content using a method of selecting the correct answer at random, B) Content using a method of selecting the correct answer sequentially, C) Error-time relationship by week of content corresponding to graph A, D) Error-time relationship by week of content corresponding to graph B.

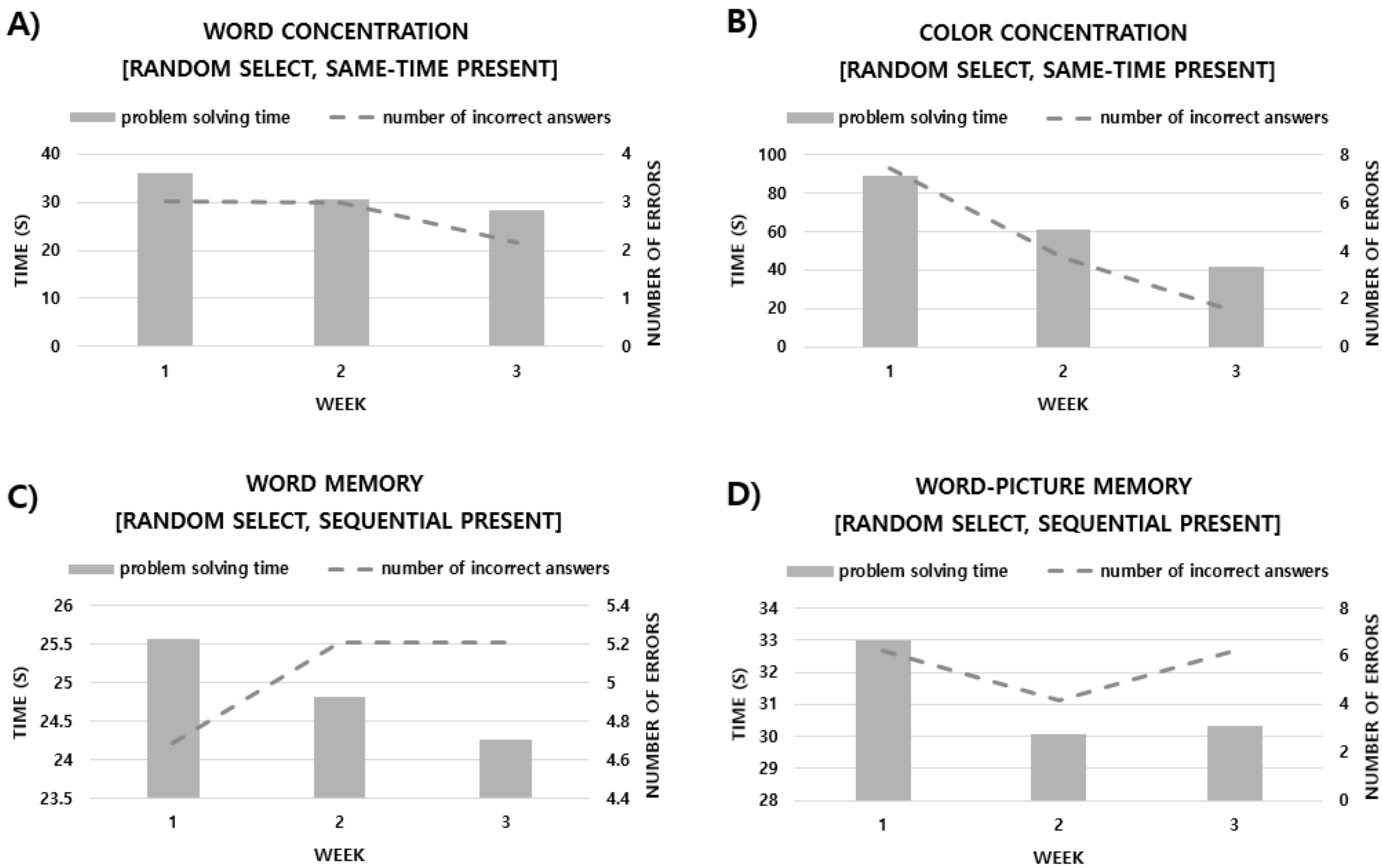

Figure 6

Comparison graph of solving time and errors of contents with different problem presentation methods among contents using random answer selection method. A) Word memory, B) Color concentration, C) Word memory, D) Word-picture memory.

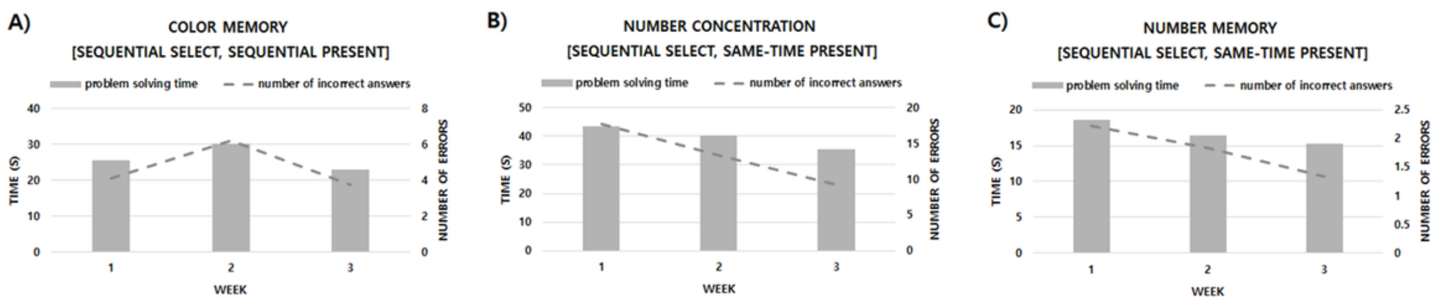

Figure 7

Comparison graph of solving time and errors of contents with different problem presentation methods among contents using sequentially answer selection method. A) Color memory, B) Number concentration, C) Number memory.

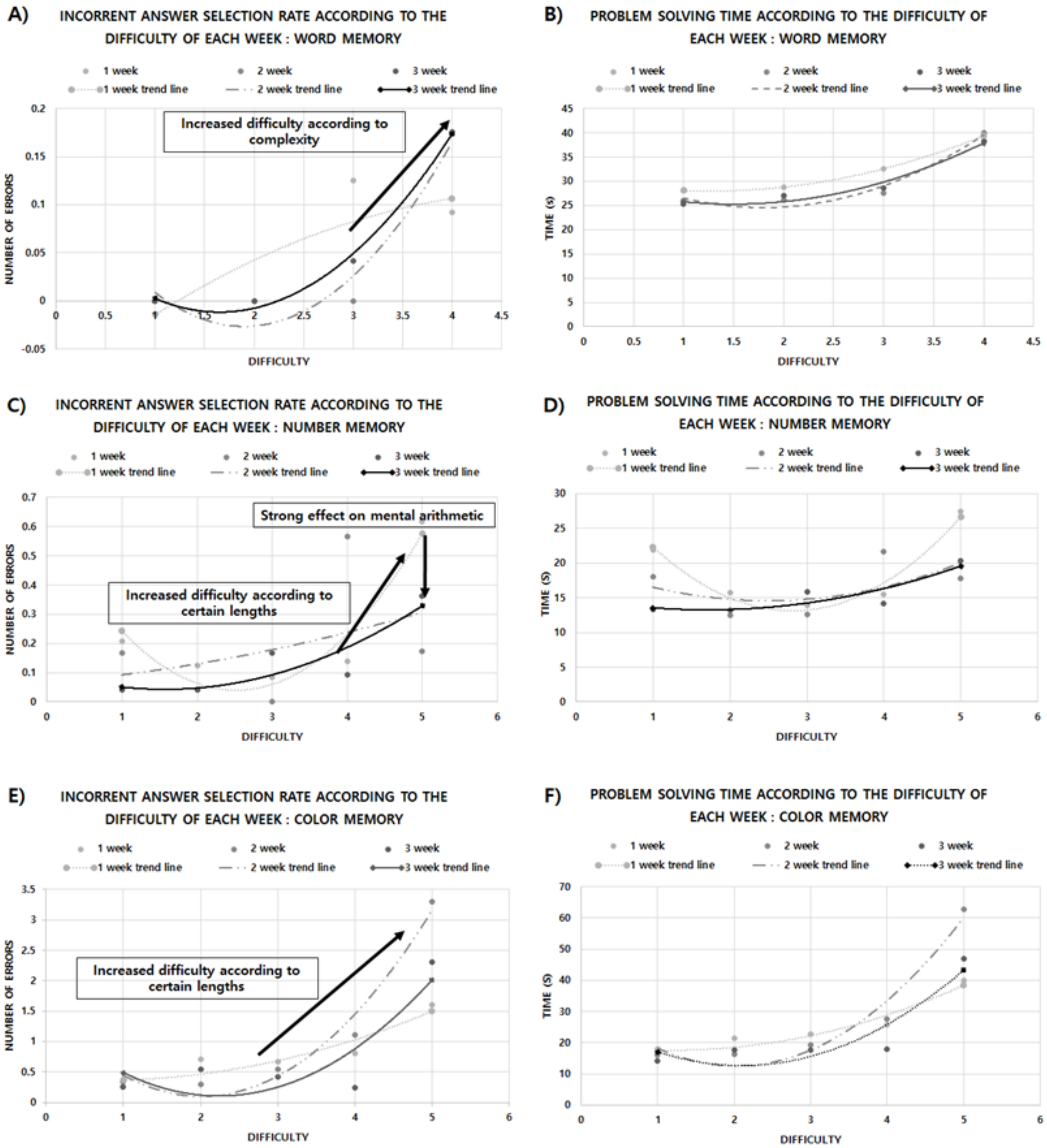

Figure 8

Incorrect answer rate and problem-solving time according to element and difficulty setting of memory training. A) and B) are word content, C) and D) are number content, E) and F) are color content.

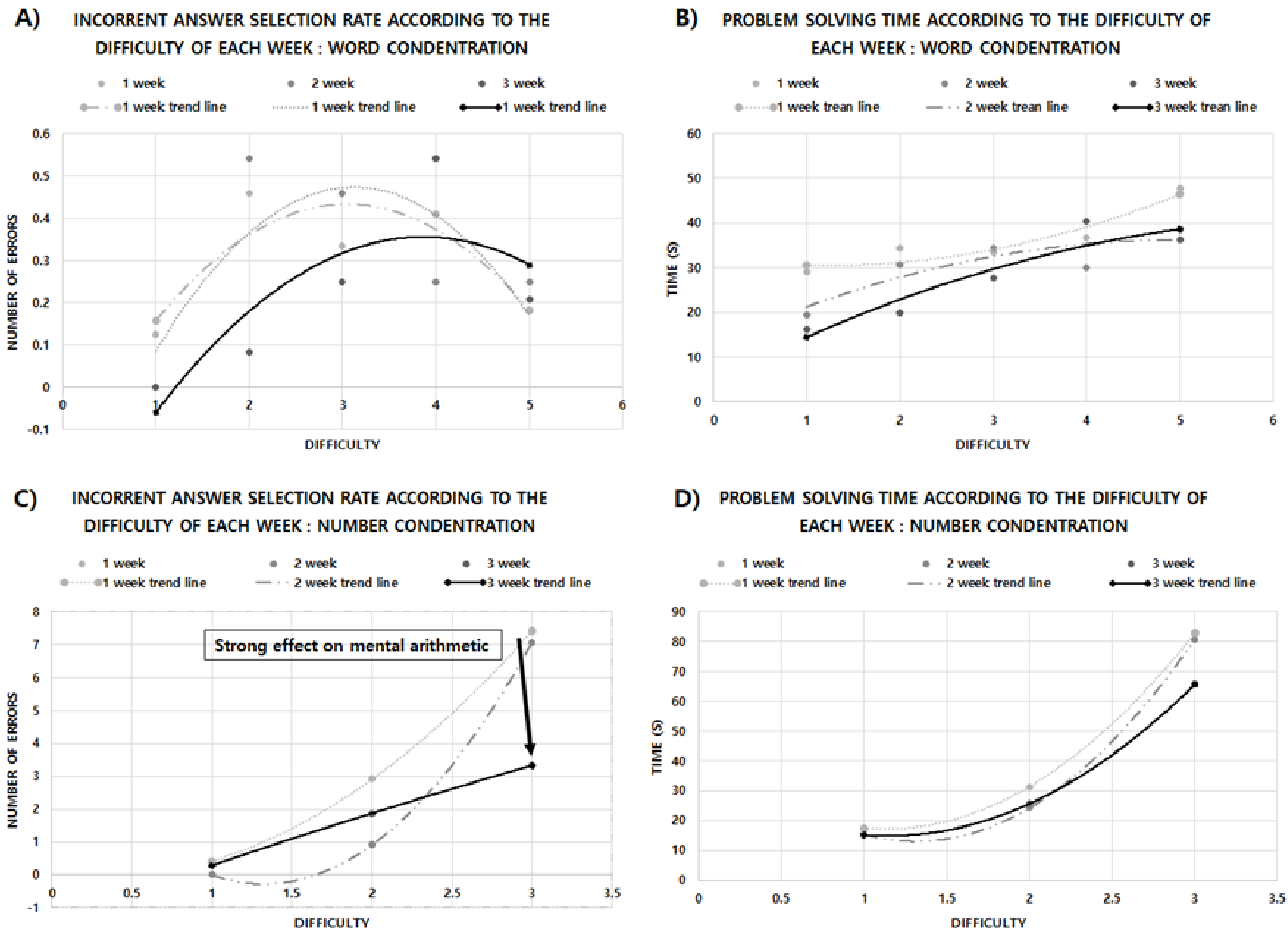

Figure 9

Incorrect answer and problem-solving time according to elements and difficulty setting of concentration training. A) and B) are word content, C) and D) are number content.