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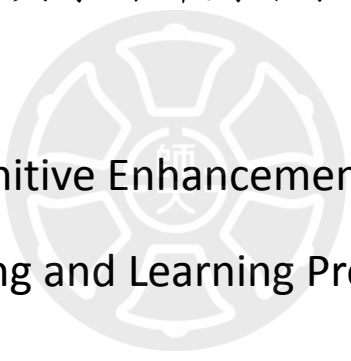
College of Science

National Taiwan Normal University

Doctoral Dissertation

透過不同的教學與學習計劃探索認知能力的提升

Exploring Cognitive Enhancement through Different
Teaching and Learning Programs



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英文摘要 English Abstract

The possibilities of cognitive enhancement have won popularity among commons and academic circles in recent decades. Cognitive enhancement has often been associated with advances in neuroscientific technologies aimed to improve cognitive and intellectual capacities of the brain. It focuses on the improvement of cognitive functions, such as attention, reasoning, memory and executive function.

Traditionally, enhancement of cognitive performance could be achieved through conventional way such as structured classroom teaching, individual learning, training (ex. abacus, foreign language, exercise), as well as the use of external information-processing devices. Contemporary attempts to improve cognitive performance often involve the consumptions of drugs, such as amphetamine, methylphenidate, and modafinil, or utilization of electrical brain stimulators.

Throughout the whole life span, the adaptations to the diverse contexts and changing social environments are very important to individuals. Capabilities of significant changes of brain and neural system in the complex environments have been referred to as neuroplasticity. During recent years, the literature on cognitive training has been growing rapidly. Neuroplasticity can be observed in mind and brain after training intervention, and the scope and pattern of training effects can be measured to identify the underling mechanism.

In general, this study aims to develop teaching and learning programs to enhance cognitive performance through the application of educational neuroscience into the optimization, generalization and integration of instructional techniques. Optimization refers to the improvement of existing techniques to achieve better results. Generalization refers to the application of existing techniques to different domains and integration refers to the combination of several existing techniques to create more effective techniques.

Topic One: Exploring Cognitive Enhancement through Teaching Programs. The design of new teaching model of neuroanatomy to prevent neurophobia in preclinical medical students.

Topic Two: Exploring Cognitive Enhancement through Learning Programs. Six-month abacus training improves working memory performance in children: a functional MRI and behavior study. Exam the effects of short term abacus training on brain structure, activation pattern and behavior, as a potential learning program to improve working memory.

Keywords: cognitive enhancement, cognitive training, neuroplasticity, teaching programs, neurophobia, learning programs, abacus training, working memory

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【Chapter 1】 Introduction

Current knowledge has enabled interdisciplinary collaboration to explore the correlation between brain and learning process (Meltzoff et al. 2009, Varma et al. 2008, Goswami et al. 2006). Each regions of the brain has its own functions which associated to certain task. More complex tasks often involve different combination of tasks and require the integration of neural activity.

Multiple neural circuits are involved in cognitive processes, such as selective attention, concentration, symbol processing, pattern recognition, working memory and problem solving (Colvin et al. 2016). The integration of these cognitive processes will form the basis of academic abilities, such as critical thinking, reading, writing, higher mathematics, social interactions, long term planning and decision-making, etc. (Figure1).

At the structural level, brain is often regarded as the integrated network of regions (grey matter) connected by the neural tracts (white matter). The neural activity associated with certain task might mainly take place in certain brain areas and be transmitted by the white matter to another part of the brain. These patterns of activity are called activation pattern. These activation patterns can be observed by functional magnetic resonance imaging (fMRI) and the functional connectivity can be observed by using resting state functional magnetic resonance imaging (rsfMRI).

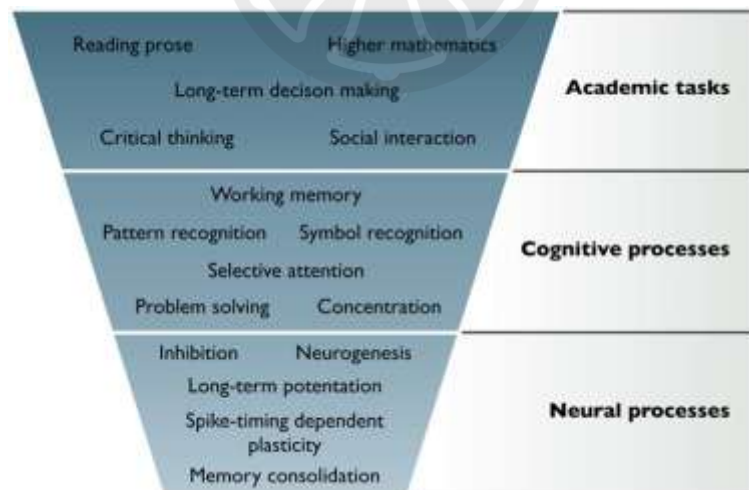


Figure1. The generation of higher level academic abilities from basic neural process, adapted from Colvin (2016). Cognitive processes are emerged from basic neural process and integrated to solve higher level academic tasks.

Cognitive enhancement

The possibilities of cognitive enhancement have won popularity among commons and academic circles in recent decades. Cognitive enhancement has often been associated with advances in neuroscientific technologies aimed to improve cognitive and intellectual capacities of the brain. It focuses on the improvement of cognitive functions, such as attention, reasoning, memory and executive function (the ability to monitor direct and coordinate various mental operations). Critical reflections on the pros and cons are essential in the booming era of cognitive enhancement.

General intelligence and cognitive performance are often associated with professional achievement. Cognitive enhancement will make more people able to meet the higher standards and potentially beneficial for people from wide range of occupational background, such as white collar worker, students, people who work in high risk, high stress environment, and shift work occupations which required extended awareness. Advancement in cognitive performance will improve quality of life and ability to contribute to society (Beddington et al. 2008). Enhanced cognitive abilities will lead to the emergence of new jobs and development of old occupations. While the benefits might seem to be individual, in the long run cognitive enhancement will eventually contribute across society by reducing cost and increasing productivity (Savulescu et al. 2011).

Traditionally, enhancement of cognitive performance could be achieved through conventional way such as structured classroom teaching, individual learning, training (ex. abacus, foreign language, exercise), as well as the use of external information-processing devices. They are often well established and culturally acceptable. On the other hand, methods to enhance cognition through unconventional means may include consumption of nootropic drugs, gene therapy, or neural implants.

Contemporary attempts to improve cognitive performance often involve the consumptions of drugs, such as amphetamine, methylphenidate, and modafinil, or utilization of electrical brain stimulators, such as transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), transcranial random noise stimulation (tRNS), and transcranial pulsed current stimulation (tPCS) (Farah 2015).

There are numbers of obstacles regarding to the development and applications of cognitive enhancement despite its potential economic and social benefits, such as the current medical system which regulate interventions for disease treatment. This system is still inadequate to regulate the application of medical treatments for enhancement purposes. The intervention that is aimed to correct certain disorder or defect of cognitive domains may be characterized as therapeutic. On the other hand, enhancement is the intervention that improves the function of the system rather than repairing specific dysfunction of certain disease. Nevertheless, therapy and enhancement is often difficult to differentiate practically (Savulescu et al. 2011). Currently, every drug available on the market that have the potential to improve cognitive performance were developed and to treat certain pathological condition.

Furthermore, the applications for cognitive enhancement need to be regular and long term but there was still not enough evidence regarding the efficacy of the cognitive enhancing drugs to improve well-being, happiness and achievements in healthy individuals and the drugs might even pose some risks (Teter et al. 2010). In addition to addiction, there are significant psychiatric, cardiovascular, and other medical risks of using drugs like modafinil and methylphenidate for cognitive enhancement. The improvement in one cognitive domain might also lead to the decrease of the performance in other cognitive domains. Therefore, proper assessment is required to determine the limits of acceptable risks and tradeoffs, such as government regulation for addictive drug for memory improvement.

People also argued that enhancements through conventional, cultural or evolutionary process are ethically not the same as enhancement using technology or medications, because they represent a new and different methodology (Schermer 2012). There are people who agree with such efforts and believe that it's the duty of each individual to enhance themselves. On the other hand, some people argue that the use of medical technologies for human enhancement may erode important human values such as dignity (Kass 2002) and solidarity with weaker groups in our society (Fukuyama 2003). It is difficult to formulate useful guidelines and policy without sufficient knowledge regarding the safety and efficacy of brain interventions. Therefore, safer and more efficient cognitive enhancement methods need to be further explored and developed.

Cognitive training

Throughout the whole life span, the adaptations to the diverse contexts and changing social environments are very important to individuals. Capabilities of significant changes of brain and neural system in the complex environments have been referred to as neuroplasticity. Interestingly, scientific findings show that the brain and mind can be plastic by training in older adults, as well as in young adults.

During recent years, the literature on cognitive training has been growing rapidly. Neuroplasticity can be observed in mind and brain after training intervention, and the scope and pattern of training effects can be measured to identify the underlying mechanism.

Educational neuroscience

Educational neuroscience is one of the fields that address this issue of cognitive training. It is an interdisciplinary field that integrates neuroscientific research to educational practice and policy (Figure2). It studies the mechanisms between education and its associated changes in the brain and behavior. These changes are not only observable in the behavioral level, but lead to brain reorganization in the functional, anatomical, cellular, and molecular levels. The changes might include the change in synaptic strength (Feldman et al 2012), through the growth of new neurons (Murphy et al 1991, Vulkovic et al 2013), or changes in the neuron themselves (Buonomano et al 1995). They can occur in grey matter as well as white matter. These cumulative changes may improve the processing speed within regions, communication speed between regions and

eventually lead to enhancement of cognitive performance.

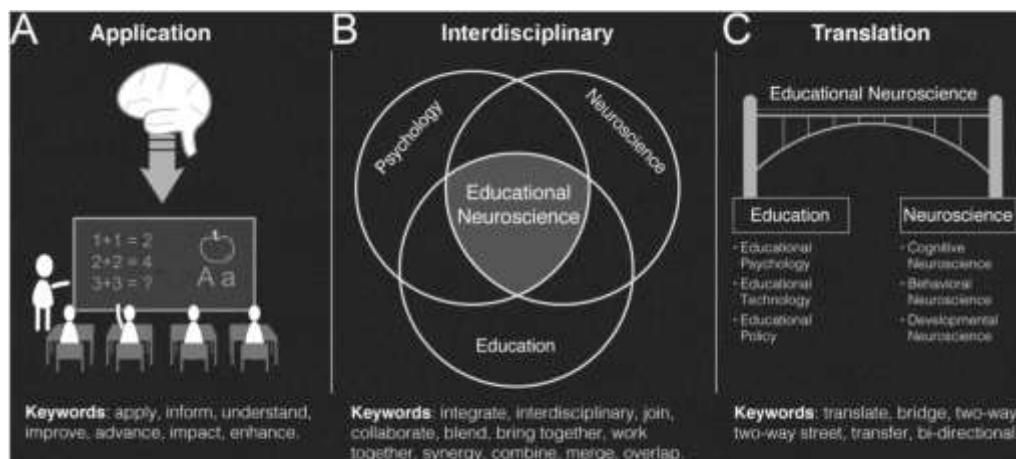


Figure2. Three major themes of educational neuroscience: (a) application of neuroscience discoveries in the classroom, (b) overlapping and interdisciplinary collaboration of psychology, neuroscience, and education, and (c) a bridge that translates between education and neuroscience, adapted from Feiler et al. (2018).

Neuroscience and education can interact directly by considering the brain as an organ with certain requirements for it to learn and reorganize optimally or indirectly as neuroscience shape psychological theory and psychology influence educational practices (Feiler et al. 2018). Successful learning often requires complex processes and attention to multiple domains such as cognitive, affective (emotion, motivation), social (interpersonal interaction), environmental (location and condition) as well as metacognitive domains (Young et al. 2014).

Cognitive Load theory

Cognitive Load Theory (CLT) is one of the theories that have been suggested to overcome these challenges of successful learning. CLT aims to integrate memory systems (sensory, working and long-term memory) and the cognitive load imposed on working memory (WM) into the learning process (Sweller 1988). This theory recognized the limited capacity of WM as obstruction to long term memory formation and focus to improve the learning process by optimizing the utilization of WM. CLT suggests that there are three types of load imposed on the WM during the learning process which include intrinsic, extrinsic and germane load (Figure3, 4).

Intrinsic load refers to the load associated with the learning task. The knowledge of the individual, number of information elements need to be learned and the interaction between those elements can affect the intrinsic load. Higher number of elements and lower elements interactivity will increase the intrinsic load on WM. Intrinsic load can be managed by simplifying the information to be learned or enhancing the expertise of the learners by providing preparatory training prior to the task.

Extraneous load refers to the load imposed upon the trainee's WM but not necessary for learning

the task at hand. This load can emerge from insufficient guidance that caused the learners need to use their own ineffective methods to learn or find information. It can emerge from the separation of teaching materials into several places, time (across different lectures) or when the visual or auditory channel is overloaded. Finally, the distractions or tasks unrelated to the learning process can also be the source of extraneous load.

Germane load refers to the load imposed by the mental processes necessary for learning to occur, such as the schemata and automation formation. Germane load can be viewed as the learner's level of concentration devoted to learning in addition to the intrinsic load associated with holding the relevant interacting elements in WM. Germane load is regulated by the individual and when the extraneous and intrinsic load are too high there will be insufficient WM resources available for learning. Most importantly, cognitive loads are additive, cognitive performance will be impaired and learning process will be harmed if the total load exceed the WM capacity. Therefore, better teaching and learning programs need to be developed to help students to overcome this problem.

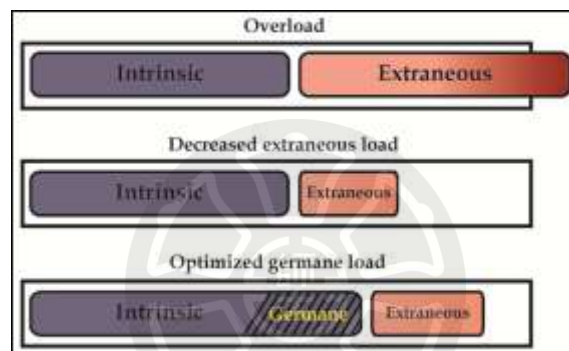


Figure3. Composition of cognitive load imposed to working memory, adapted from Inkster (2018).

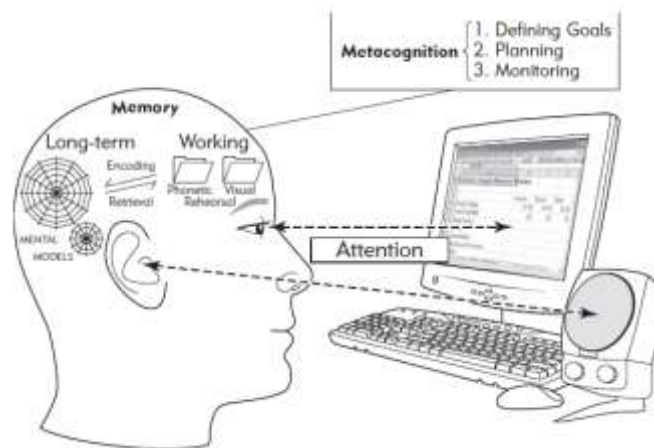


Figure4. Human learning process, adapted from Clark (2008).

Specific Aims of Thesis

In general, this study aims to develop teaching and learning programs to enhance cognitive performance through the application of educational neuroscience into the optimization, generalization and integration of instructional techniques. Optimization refers to the

improvement of existing techniques to achieve better results. Generalization refers to the application of existing techniques to different domains and integration refers to the combination of several existing techniques to create more effective techniques.

Aim One: Exploring Cognitive Enhancement through Teaching Programs

1. Topic: The Design of New Teaching Model of Neuroanatomy to Prevent Neurophobia in Preclinical Medical Students.
2. This study aimed to further explore cognitive enhancement effects through the implementation of virtual reality technology into the teaching curriculum of neuroanatomy, especially to overcome neurophobia.

Aim Two: Exploring Cognitive Enhancement through Learning Programs

1. Topic: Six-month abacus training improves working memory performance in children: a functional MRI and behavior study.
2. Exam the effects of short term abacus training on brain structure, activation pattern and behavior, as a potential learning program to improve working memory.



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【Chapter 2】 Exploring Cognitive Enhancement through Teaching Programs

The Design of New Teaching Model of Neuroanatomy to Prevent Neurophobia in Preclinical Medical Students

Abstract

Human anatomy has been regarded as the keystone of medical knowledge for centuries. Cadaver dissection is the prevailing pedagogy adopted in most medical schools for anatomy learning. However, with the rise of new computer technology, radiology and digital medical images provide an alternative perspective to approach human anatomy. Hence, “Can traditional cadaver dissection be replaced by new computer-based anatomy teaching?” must be inquired. Here, we also try to explore the role of virtual reality in anatomy teaching. This study reviews and analyzes the current literatures in terms of anatomy education worldwide. We aim to look into the challenges most medical students confront in learning anatomy, and further provide a valid teaching strategy to diminish the current gap in between basic and clinical anatomy.

Background:

Neurophobia, being described as “a fear of the clinical neurosciences”, is a longstanding problem among preclinical medical students. The lack of knowledge in the complexity of neuroanatomy is regarded as one of the most important reasons. Therefore, a new teaching model of neuroanatomy was developed.

Summary of work:

We combined traditional method and contemporary virtual reality technologies to design this new teaching model of neuroanatomy, including anatomical atlas sketch, pretest and posttest of reading brain computed tomography scans, and teaching with dextroscope. During July 2009 and July 2010, fifty-five medical students in Taipei Medical University Hospital were enrolled in our study.

Summary of results:

The significant improvement between the mean scores of pretest and posttest was observed. Questionnaire results revealed that most of the students express strong positive attitude toward learning in dextroscope, and the teaching model of neuroanatomy. Moreover, they also showed more confidence on learning neuroanatomy after being taught with dextroscope.

Conclusion:

A carefully designed teaching model of neuroanatomy could possibly help medical students to overcome neurophobia. Besides, dextroscope is a friendly learning environment of virtual reality.

Take-home messages:

The traditional method of teaching neuroanatomy could be integrated with new virtual reality technologies to innovate a curriculum of the future.

Keywords: anatomy education, cadaver, computer, clinical anatomy, virtual reality

Introduction

Anatomy has been the fundamental medical knowledge for centuries since renaissance, but the teaching of anatomy is facing significant challenges in recent years. A great leap in the development of digital medical images has provided new ways to see through the structure of the human body. With the rapid advances in information technology, the role of diagnostic radiography in anatomy education is expanding [1]. Many reports had pointed out the potential roles of digital medical images to enhance the teaching and learning of anatomy [1, 2].

However, there is a developing debate on methods of teaching anatomy. The use of cadaver dissection is still a traditional and important part in the Anatomy course for medical students. But, could it be totally replaced by computerized anatomy resources, (including diverse software and websites)?

Rapid evolution of three-dimensional images technologies has made virtual environments (VEs) possible in recent years. The applications of virtual reality (VR) on health care are diverse, including surgical planning and simulation, medical education, patient simulator, psychological assessment, rehabilitation, bronchoscopy, et al [4]. The applications of virtual reality (VR) in surgery include anatomy education, preoperative planning and simulation, and assessment of surgical skills.

The results of applications of VR techniques in preoperative planning and simulation are promising, especially for laparoscopic surgery and neurosurgery [4, 5, 6]. The task performance in simulator is strongly correlated to daily surgical performance [7]. The implementation of VR in anatomy education also has great potential, but could it influence the learning of reading skills of diagnostic images for medical students?

Moreover, the role of virtual reality (VR) in the teaching of anatomy is revolutionary and with great potential [3, 4]. Since the Visible Human Project (VHP) launched by the US National Library of Medicine in 1988[11], it allowed the developments of various VR 3-D models. The most renown is the Visible Human 3D Anatomical Structure Viewer (EPA Lausanne) [12].

3-D visualization of clinical diagnostic images allows a deeper understanding of spatial relationships between deep structures that hardly can be achieved by other teaching methods [4]. Taking brain neuroanatomy as an example, trainees thus can see the sophisticated and delicate neural structures by dynamic dissections from various directions with the help of VR.

VR definitely improve the learning of anatomy. But, could the VR techniques influence the learning of reading skills of radiological anatomy (diagnostic images) for medical students?

Radiological anatomy is totally different from gross anatomy. Medical images are another representation of gross anatomy, and anatomy knowledge gathered from dissections always needs being translated into cross-sectional views of clinical images [11]. That is why students often feel frustrated while reading cross-sectional clinical images (such as, brain computed tomography scans) at the first moment.

Therefore, appropriate learning scaffolds are needed as the bridges of knowledge among those different representations of anatomy.

The learning of reading brain computed tomography (CT) scans is a critical step in studying clinical neuroscience, but it seems to be a major obstacle to medical students. The most difficult parts are lack of the acquaintance of medical terms and 3-D concepts of neuroanatomy.

Therefore, we are developing a new model of teaching clinical neuroanatomy for preclinical medical students. The teaching model includes sketch of atlas of neuroanatomy, self-directed learning of reading brain computed tomography (CT) scans, and implement of dextroscope. We are in the hope to teach gross anatomy in the context of clinical setting.

Sketch is an unique skill commonly used in medicine, and it is especially important in the training of surgery. Students have to recognize what structures they are going to sketch, and allocate them in a proper position after knowing the spatial relationship between neural structures. Sketch could help students to recall the unfamiliar and difficult neuroanatomical terms, and restructures 3-D concepts of neuroanatomy inside students' minds.

Dextroscope (Volume Interactions, Ltd., Singapore) is a virtual reality system for preoperative planning and simulation of surgery. Patient-oriented and fused medical images are presented stereoscopically and the fused images can be manipulated freely from various dimensions. Some degree of simulation of bone drilling and brain retraction can be implemented in the dextroscope. With the help of dextroscope, students can trace vascular and neural structures in dynamic serial images, and further establish a deep understanding of the spatial relationships between individual structures.

This new model of teaching clinical neuroanatomy definitely encourage students to learn clinical neuroanatomy in a more interesting and promising way. However, we also want to see if we could improve the learning of reading skills of brain computed tomography (CT) scans with the help of dextroscope ? Part of the aim of our study is to see if VR can improve students' confidence of reading brain CT scans.

What is Neurophobia?

Neurophobia is described as “the fear of clinical neurosciences”. It is a worldwide phenomenon among medical students [13].

Neurological diseases are becoming more and more popular. Brain computed tomography (CT) scans gave become a regular and screening scans for diagnosing neurological problems. Learning to read brain CT scans is the crucial first step to learn clinical neurosciences.

However, atlas in anatomical textbooks and brain CT images are different representations of neural structures. Medical Students' memory battery for neuroanatomy is very poor. Students have difficulty to have far transfer of anatomical knowledge, which was learned years ago.

Therefore, an integrated program is needed to path the ways for the learning of basic and radiological neuroanatomy. The aim of this study was to evaluate the impact of dextroscope on

the learning of radiological neuroanatomy, and to verify that if virtual reality simulator, dextroscope, could help the learning of reading brain computed tomography scans.

Methods

Sixty-five preclinical medical students in Taipei Medical University Hospital were enrolled in this study. All of the successive students rotate in the department of neurosurgery for two weeks, and they are divided into two groups. The implement of dextroscope is used as a treatment for the students of the group one.

Thirty-five students are in the group one, and the timetable of teaching activities is as the following. On day1, and day 2 of the rotation, students are asked to sketch atlas of basal ganglia and brain stem, and the terms of neuroanatomy structures will be indicated. Then they need to complete a self-study brain CT scans test (including fifty questions), as the pretest, during the first week rotation, and their answers will be discussed with teacher on the 8th day. Dextroscope will be taught for one hour on day 5 and another hour on day 13 of the rotation. The post-test of brain CT scans is held on day 13 after the teaching of dextroscope finished.

Thirty students are in the group two, and the timetable of teaching activities is as the following. On day1, and day 2 of the rotation, students are asked to sketch atlas of basal ganglia and brain stem, and the terms of neuroanatomy structures will be indicated. Then they need to complete a self-study brain CT scans test (including 50 questions), as the pretest, during the first week rotation, and their answers will be discussed with teacher on the 8th day. The post-test of brain CT scans is held on day 13. Dextroscope will be taught for one hour, as salvage instruction, only after the post-test of brain CT scans being finished.

Learning attitude questionnaire and self-confidence questionnaire are completed after the rotation. Degree of satisfaction is divided into five grades.

The fifty questions of pretest of brain CT scans include thirty questions of neuroanatomy and twenty basic clinical questions. Full score of the fifty questions is one hundred.

The composition of the fifty post-test questions is slightly different from the pretest's. Seven advanced clinical questions are added, and they are deployed to indicate the problem-solving ability of students. Therefore, the fifty post-test questions are composed of twenty-six questions of neuroanatomy, seventeen basic clinical questions, and seven advanced clinical questions. Full score of the post-test is also one hundred.

Results

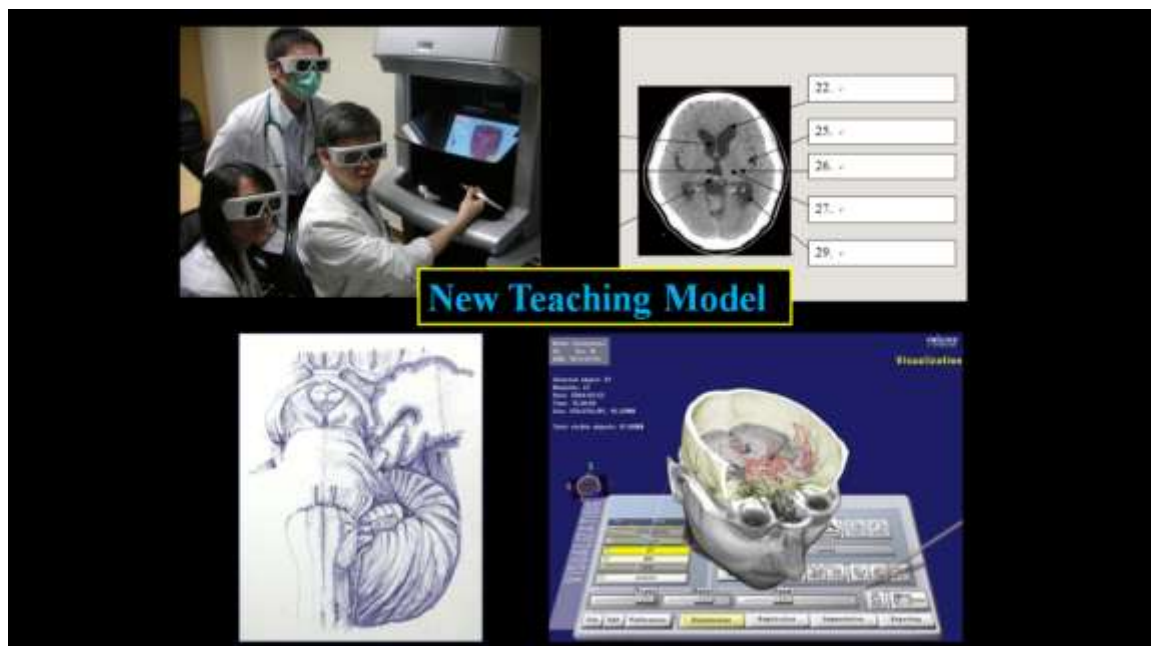
Table 1. Results of sixty-five students

	Mean	SD	Rate of correct Answers
Pre-test	71.29	8.4	Full mark : 100
Post-test	89.91	6.3	
Clin. A (7tests)	8.46	2.42	60%
Clin. B (17tests)	31.94	2.74	94%
Anat. (26tests)	49.24	3.47	95%

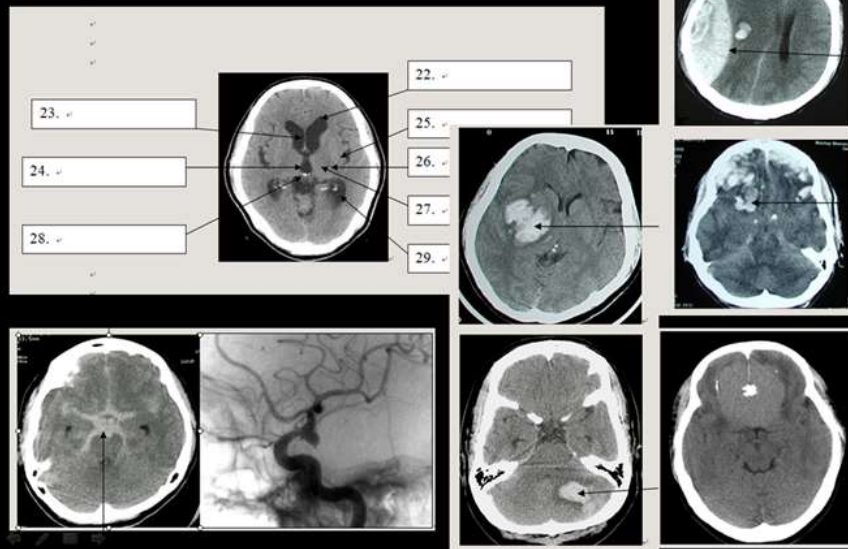
E.S. (Cohen's D): 2.53 : huge effect size.

Table 2. Results of different groups.

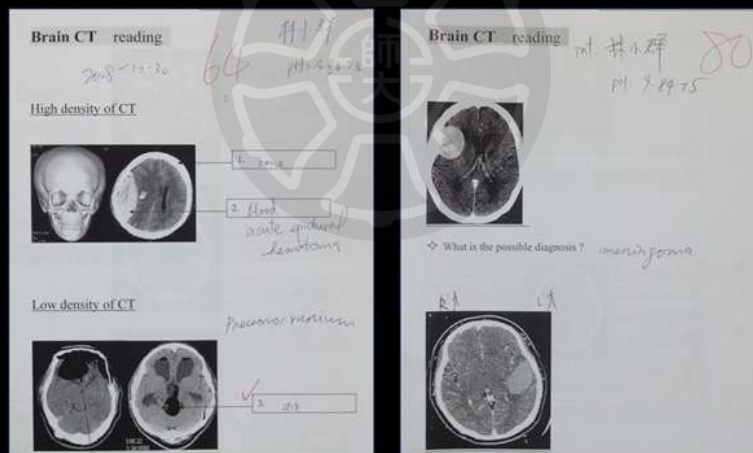
	Treatment	Pretest score	Post-test score	Score Increment
Group one	With Dextroscope (35 students)	71.9	90.0	18.1
Group two	Without Dextroscope (30 students)	66.8	87.9	21.0



Structured Learning



Pre-test Post-test



Discussion

Besides cadavers and dissecting room, there are emerging methods of teaching gross anatomy with the generalization and advance of computer technology [1, 2, 3, 4]. But, could cadaver dissection be totally replaced by computerized anatomy resources? Biasutto et al. (2006) argued that there were no objective and scientific data to prove the superiority of computerized resources over cadaver dissection, and demonstrated that the best way of teaching anatomy is the combination of cadaver dissection and computerized materials [2].

There are three major applications of virtual reality (VR) on health care: anatomy education, simulation of operation, and radiology education.

The application of virtual reality (VR) has led anatomy education into different horizon [3, 4, 5]. Through interactive 3-D graphics, students can explore internal structures in various dimensions. Anatomical structures are represented in dynamic images, and it allows trainees to trace all kinds of tissues from multiple viewpoints [4]. Therefore, students can attain a deeper understanding of spatial relationships between different structures that cannot be achieved by other teaching methods.

The simulation of operation in virtual reality (VR) environments has been introduced successfully in recent years, especially in laparoscopic surgery and neurosurgery [4, 5, 6, 8, 9, 10]. With the advances of endovascular techniques and radiosurgery, there are more alternative methods of treating cerebral aneurysms or skull base tumors. The decrease of open operative cases is making young neurosurgeons more difficult to develop their surgical skills [8]. VR technologies provide a no-risk environment for preoperative rehearsal, and it allows residents to simulate operation preoperatively. Therefore, neurosurgeon can somehow keep experienced in those rare and complicated surgeries with the implement of VR technologies.

Nonetheless, virtual reality is never like actual surgery. It allows some degree of rehearsal of bone drilling, brain retraction, and simulation of possible trajectory and probable difficulties encountered during operation. However, all of these advantages are the initial steps of performing surgery. In real life, the unpredictability during actual operation is more challenging. The experience in computerized simulator could not offer similar tactile and emotional training from the real world experience.

Significant progresses in medical imaging in recent years have enhanced the potential role of radiology over anatomy education. Since the introduction of Visible Human Project (VHP) by National Library of Medicine (NLM) in 1988[26], digital diagnostic images can be processed in various ways. Medical images are restructured in 3D style, and it has made virtual reality resources available for radiology education. Students now can see the structures in a more comprehensive way, and spatial relationships between structures could be realized nearly without any limitation. But, could the VR techniques improve the learning of reading skills of clinical images, ex. brain CT scans, for trainees?

The design of our new teaching model for neuroanatomy adopted sketch (the traditional learning method) and dextroscope (VR technology) to facilitate students' learning of reading brain CT scans. From our preliminary results, there are no differences of average marks and improvement between study and control group. The treatment for this teaching model, dextroscope, seems to have no role on the learning of reading brain CT scans. However, based on the primitive results of the learning attitude questionnaire and self-confidence questionnaire, students do feel direct help and deeper understanding of spatial relationships between structures from the teaching of dextroscope, and they also show more confidences on the following learning of clinical neuroscience.

The significant improvement between the mean scores of pretest and posttest was observed. Questionnaire results revealed that most of the students express strong positive attitude toward learning in dextroscope, and the teaching model of neuroanatomy. Moreover, they also showed more confidence on learning neuroanatomy after being taught with dextroscope.

Conclusion

Our new teaching model for neuroanatomy seems to enhance the learning of reading brain CT scans. A carefully designed teaching model of neuroanatomy could possibly help medical students to overcome neurophobia. Besides, dextroscope is a friendly learning environment of virtual reality. Therefore, the traditional method of teaching neuroanatomy could be integrated with new virtual reality technologies to innovate a curriculum of the future.

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【Chapter 3】 Exploring Cognitive Enhancement through Learning Programs

Six-month abacus training improves working memory performance in children: a functional MRI and behavior study

Abstract

Abacus experts have demonstrated extraordinary potential of mental calculation. It was reported that non-experts mainly showed activity in the prefrontal and perisylvian areas, while experts with long-term training of at least three to five years, showed more activation over premotor and parietal regions. It has also been reported that abacus-based mental calculation (AMC) training was able to improve the working memory. Nevertheless, most of previous studies adopted cross-sectional designs to evaluate the results.

The aims of our study are to evaluate the relatively short term effect of a six-month abacus-based mental calculation (AMC) training on the functional connectivity network, and to investigate the possibility of AMC training effect transferring to untrained working memory tasks. A total of 70 human subjects were assigned to abacus (ABA) or control (CON) groups. The ABA group received 3.5 h AMC training per week for 25 weeks, whereas the control group performed general reading exercises. The total effective training time was 87.5 hours. This longitudinal study utilized standardized tests, including functional MRI (fMRI), and resting state fMRI. The validity and scale of this change were evaluated on both the behavioral level and the functional level under a relatively short-term training curriculum.

The results from post-training abacus (ABA) group showed that there were significant improvements in working memory index and serial addition reaction time. Functional MRI results revealed tendency of a shift in the activation when performing mental calculation task from prefrontal to the parietal regions. Regression analysis of functional connectivity and working memory index revealed that there was a significant correlation between working memory index and functional connectivity of left Broca area and left angular gyrus ($n = 21$, $r(19) = 0.429$, $p = 0.041$). The correlation between working memory index and functional connectivity of left Broca area and left inferior frontal gyrus (proximal) also trended toward significance from ($n = 21$, $r(19) = 0.085$, $p = 0.666$) to ($n = 21$, $r(19) = 0.386$, $p = 0.069$). These combined results suggested that six months of AMC training can generalize to improvement on untrained working memory tests, and a midway paradigm shift (paradigm drift) can be expected along the fronto-parietal circuitry within the relatively long time required to become an expert.

Compared to the common practice of task repetition, AMC training is a more complex and interesting method of working memory training with a stronger sense of self-accomplishment through its step-by-step training curriculum. AMC is not only an arithmetic operation, but it might also be an appropriate learning tool to improve working memory capabilities by exercising

visuo-motor and visuo-spatial skills, as partially evidenced by the current study. As a result of this educational neuroscience study, we might be able to start taking a different perspective on the traditional Chinese tool for not only calculation but also learning potential in the modern age.

Keywords: abacus, abacus-based mental calculation, functional connectivity, resting state, working memory, working memory training

Introduction

With a history tracing back various millennia in different cultures, the abacus is an essential tool to human civilization growth and development. It is also a significant symbol in Chinese culture for trade and calculation. Inscription of Chinese abacus on the Representative List of the Intangible Cultural Heritage of Humanity was announced on December 2013 by UNESCO for its cultural significance and "training in abacus-based mental arithmetic is thought to improve a child's attention span, memory and mental capability." (1).

Abacus experts have demonstrated extraordinary potential of mental calculation (2), and even beginner youths are often expected to improve in attention and mental focus abilities. Past imaging studies show a significant difference between experts and non-experts in brain functional areas when performing mathematical tasks (2-5). Non-experts show activity in the prefrontal and perisylvian areas, while experts with long-term training show more activation over premotor and parietal regions.

Most abacus-related studies in the past have cross-sectional designs, comparing abacus experts with non-experts. However, in the current Chinese social norm, with the availability of more active or creative extracurricular courses, very few children have the opportunity or willingness to pursue further abacus training after the initial one to two years, far less than the necessary training to become an expert. Therefore, we are curious about the effects of short-term abacus training on functional and behavioral levels. More importantly, how soon can we expect change after initializing training on the functional level and the behavioral level?

Children in Chinese society are encouraged to study for at least six months to one year to become acquainted with abacus-based mental calculation (AMC) and express significant behavioral improvement. The Chinese Abacus Association in Taiwan states that according to past experience, the greatest level of behavioral improvement is shown after six months to one year. Irwing et al. suggested in 2008 a general intelligence improvement after receiving only 34 weeks of abacus training (6). Hu et al. suggested in 2011 potential enhancement on white matter integrity after abacus training for 3 years (7). Takeuchi et al. showed in 2013 that cognitive training can have probable effects on intrinsic brain activity and connectivity (8).

Therefore, in this study, we hypothesize potential midway paradigm drift, significant change in visuo-motor and visuo-spatial regional connectivity, and working memory behavioral

improvement within a six-month abacus training period. After deploying standardized tests, functional MRI (fMRI), and resting state MRI (rsMRI), we evaluate the validity and scale of this change on both the behavioral level and the functional level under a relatively short-term training curriculum.

Methods

The fMRI scanning experiment of this study was performed in Taipei Wanfang Hospital. The total number of subjects was 70. The duration of this study was about half a year and two fMRI scans will be performed in total.

Twenty-seven children in total were excluded from the data analysis due poor quality MR images ($n=27$). A total of forty-three healthy right-handed children data were analyzed in this study. The subjects are split into two groups: abacus training (ABA, $n=21$, 17 females, mean age = 9.61 years) and reading control (CON, $n=22$, 16 females, mean age = 10.57).

研究程序:

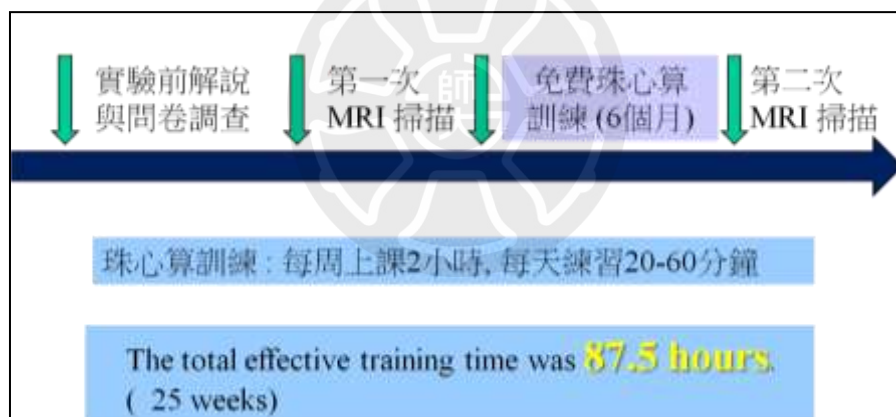


Figure 1. Research procedures.

Two abacus-based mental calculation (AMC) teachers were recruited to provide training for the ABA group over a six-month period. The group received 3.5 hours of training per week (2 hours of teacher-student lessons and 1.5 hours of practice homework) for 25 weeks. The CON group performed general reading exercises for 3.5 hours per week for 25 weeks. The total effective training time was 87.5 hours.

在每次fMRI影像掃描之前，會先在萬芳醫院，進行核磁共振攝影試驗前說明，約需二十分鐘。每次的功能性核磁共振fMRI影像掃描約需四十分鐘，包括第一部分的腦部結構檢查與第二部分執行心算任務時的掃描。在影像掃描時所進行的任務 (task) 有兩種，包括簡單與複雜的十個數目字的累加計算能力檢測，以及空間能力檢測。

珠心算訓練為期6個月，在受訓期間，每個星期需接受2小時的珠心算訓練，且每天您須自

主練習由試驗主持人所提供的珠心算練習題，每天20分鐘至30分鐘。且在受訓期間，您不能接受其他心智或學術的訓練課程。

在珠心算訓練六個月後，將立即進行第二次的功能性核磁共振fMRI攝影。

試驗程序

- ☐ 第一次核磁共振攝影試驗前說明：約需 20 分鐘
- ☐ 第一次核磁共振攝影：約需 40 分鐘
- ☐ 第一次數算能力及空間能力測驗：約需 30 分鐘
- ☐ 第一次工作記憶能力測驗：約需 30 分鐘
- ☐ 家庭與學習背景問卷調查：約需 20 分鐘
- ☐ 珠心算訓練：6 個月
- ☐ 第二次核磁共振攝影試驗前說明：約需 20 分鐘
- ☐ 第二次核磁共振攝影：約需 40 分鐘
- ☐ 第二次數算能力及空間能力測驗：約需 30 分鐘
- ☐ 第二次工作記憶能力測驗：約需 30 分鐘

MRI 試驗程序

Table 1. MRI experiment procedures

fMRI 掃描前解說	20 min	
RS-MRI	6 min	
Task-fMRI	15 min	MC (10.5 min) MR (4.5 min)
T1 (3D)	7 min	
DTI	8 min	
fMRI 掃描後測驗		
MC test	10 min	
MR test	20 min	Purdue (前10題)
Working memory test	15 min	魏氏

The subjects were examined with fMRI, rs-fMRI functional connectivity (FC), and behavioral exams before and after the six-month training period. Abacus rating exams for the ABA group were provided at the end of the training period by the Chinese Abacus Association.

Image acquisition and preprocessing

The subjects were asked to perform a simple serial addition task (SSA) during the fMRI scan. The task initialized with the presentation of a crosshair of 15 seconds, followed by a control or

task period of 24 seconds. There were four control and four task blocks in a run. The control block included ten eight-digit random numbers presented in series with frequency of 0.5 Hz and subjects were required to gaze at the numbers without calculation. The block was then ended by a 4-s period of presenting two numbers and the subjects were asked to randomly select one number by a mouse-click. The task session presented ten random one-digit numbers with the same frequency and the subjects were instructed to sum the presented digits. At the end of each task block, the subjects were asked to select by mouse-click the correct sum from a 4-s queue of two numbers. During the rs-fMRI scan, subjects were instructed to keep their eyes closed, remain clear-minded, and think of nothing in particular.

Table 2. Experimental design of the task.

		+	Task : 10 個數字連加	請作答
Seconds		15	20	4
Control group		15	8 位數	4
SSA		15	1 位數	4
CSA	Non	15	2 位數	4
	Expert	15	4 位數	4

☐ Dummy + blank: 8 seconds
☐ 4 cycles = $78 \times 4 = 312$ seconds

The fMRI images were acquired with a 1.5 T MAGNETOM Avanto system (Siemens Healthcare, Erlangen, Germany) using a T2*-weighted gradient-echo echo-planar imaging (EPI) sequence (TR/TE/FA = 3000 ms/50 ms/90°). For each subject, 104 volumes of 20 axial slices per volume were acquired. Resting state acquisitions were performed with the same sequence and parameters except TR = 2000 ms and total volume = 180.

Functional images analyses were performed by using SPM5 (9) and REST (10). The EPI data was realigned and spatially normalized into MNI template, then smoothed with a Gaussian kernel of 6 mm. Functional activations were obtained by modeling the data with GLM and group results were analyzed using one sample t-test. For rs-fMRI, after preprocessing, FC images underwent seed-based correlation analysis. Left prefrontal seeds were selected from the results of a task-related fMRI pilot study (11) (Table 1) including left fronto-insular cortex and left Broca area (LBA). The correlated results were transformed to approximate Gaussian distribution using Fisher's z transformation. Between-group and within-group comparisons were assessed by two-sample and paired t-tests, respectively. For regression analysis, the ROIs were selected from

activated prefrontal and parietal clusters within left inferior frontal gyrus (LIFG) and left angular gyrus (LAG), respectively, as determined using the anatomical automatic labeling (AAL) template (12).

Behavioral measures.

After each image acquisition, the WISC-IV exam's working memory subtasks (including digit span, letter-number sequencing, and arithmetic subtests) were deployed to examine the subjects' working memory capabilities, and an anxiety score questionnaire was used to evaluate the level of anxiety the subjects felt towards mathematical processing and towards the MRI examination.

Statistical analysis

Paired two-tailed t-tests were performed to compare the differences of means between pre- and post-intervention tests. Meanwhile, the effect size is specifically computed by using Cohen's *d* coefficient. Behavioral and functional connectivity correlations were performed using Spearman's rank correlation.



Results

Behavioral results

Table 3. Working memory performance results of the ABA and CON group

		Memory span	Number sequence	Math.	WM Index
ABA, n=21	Pre-intervention	10.38 ± 3.07	9.43 ± 3.88	9.35 ± 2.68	125.00 ± 23.77
	Post-intervention	10.90 ± 2.81	10.33 ± 2.48	9.95 ± 2.65	131.35 ± 19.14
	Δ	0.52	0.90	0.60	6.35
	Δ (%)	5.05 %	9.60 %	6.42 %	5.08 %
	P-value	0.2129	0.1811	0.1020	0.0369
	Cohen's d	0.09	0.28	0.23	0.30
CON, n=22	Pre-intervention	10.32 ± 3.54	10.00 ± 3.01	8.82 ± 3.20	126.68 ± 22.92
	Post-intervention	10.82 ± 3.30	10.50 ± 2.50	9.32 ± 3.15	129.95 ± 21.62
	Δ	0.50	0.50	0.50	2.91
	Δ (%)	4.85 %	5.00 %	5.67 %	2.30 %
	P-value	0.2207	0.4026	0.5807	0.4475
	Cohen's d	0.15	0.18	0.16	0.15

On the IQ test WISC-IV exam's working memory subsection, the Abacus group (n = 21) advanced 6.35 marks (from 125 to 131.35) on working memory index (WMI). The WMI results revealed significant change after training ($p = 0.0369 < 0.05$, Cohen's $d = 0.30$). Meanwhile, the control group did not revealed significant change ($p = 0.4475$, Cohen's $d = 0.15$), and it advanced only 2.91 marks (126.68 to 129.59) on WMI (Table 1).

Furthermore, the abacus group expressed 1.8 times higher improvement, compared to the control group, in the word-number sequencing subtest, and it makes a 9.60% increase (9.43 to 10.33,) while the CON group made a 5.00% improvement (10.00 to 10.50).

The ABA group also demonstrated greater growth in the arithmetic subtest than the control group. Additionally, neither group showed significant improvement in the memory span subtest.

ABA group ($n = 21$) showed more concentrated distribution on box-plot, compared to CON group. (Fig. 2)

In conclusion, the abacus group showed to have a better working memory performance after abacus training for six months, and expresses significant improvement on working memory index (WMI). The abacus group showed a higher post-intervention improvement in the word-number sequencing subtest, which contributes mostly to the better working memory performance, compared to the other two subtests.

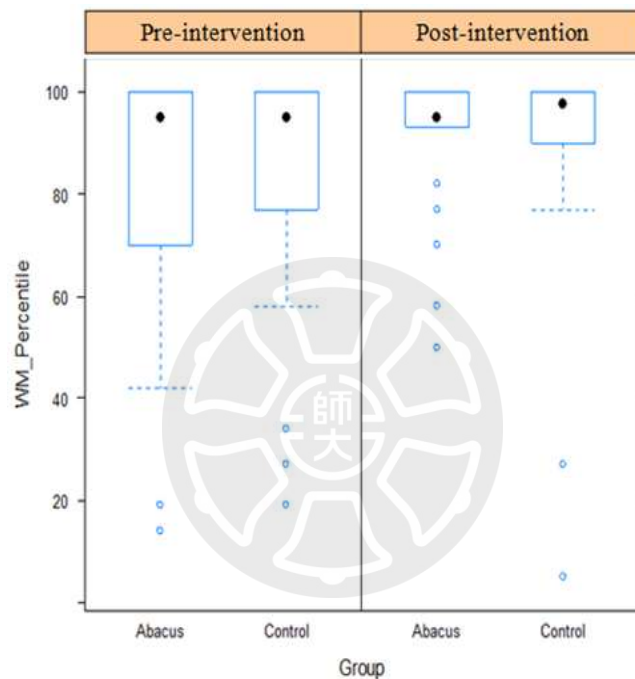


Figure 2. WISC-IV exam's working memory subsection (working memory percentile). In working memory expression, the ABA group exhibited more concentrated distribution on the boxplot after 6-month intervention.

Serial addition

Table 4. Simple Serial Addition (SSA) and Complex Serial Addition (CSA) assessment results of the ABA and CON group.

		SSA Accuracy	SSA Reaction time	CSA Accuracy	CSA Reaction time
ABA, n=21	Pre- intervention	68 % $\pm$ 23 %	1990.56 $\pm$ 497.83	62% $\pm$ 27 %	2096.85 $\pm$ 544.71
	Post- intervention	79 % $\pm$ 21 %	1618.83 $\pm$ 447.76	62% $\pm$ 26 %	2034.21 $\pm$ 556.00
	Δ	10.53 %	-371.73	0 %	-62.64
	Δ (%)	15.38 %	-18.67 %	0 %	-2.99 %
	P-value	0.1489	0.0082	0.8770	0.5153
	Cohen's d	0.51	0.81	0	0.12
CON, n=22	Pre- intervention	66 % $\pm$ 27 %	1886.94 $\pm$ 703.03	59 % $\pm$ 27 %	2078.03 $\pm$ 715.62
	Post- intervention	78 % $\pm$ 19 %	1876.33 $\pm$ 566.84	70 % $\pm$ 20 %	2275.22 $\pm$ 406.64
	Δ	12.50 %	-10.60	11 %	197.19
	Δ (%)	18.97 %	-0.56 %	19.23 %	9.49 %
	P-value	0.0873	0.406	0.1828	0.5446
	Cohen's d	0.53	0.02	0.47	0.35

There was major improvement in SSA accuracy in both abacus ($p=0.1489$; Cohen's $d=0.51$) and control group ($p=0.0873$; Cohen's $d=0.53$) and significant improvement of SSA reaction time in abacus group ($p=0.0082<0.05$; Cohen's $d=0.81$).

On the other hand, for the control group there was an 19.23% improvement in the CSA accuracy ($p = 0.1828$; Cohen's $d=0.47$), but also 9.49% increment of the reaction time ($p=0.5446$; Cohen's $d=0.35$). Furthermore, the abacus group showed an 2.99% improvement in CSA reaction time ($p=0.5153$; Cohen's $d=0.12$).

Anxiety score (AS)

Table 5. Anxiety score assessment result of ABA and CON group

		AS (Prescan)	AS (Math)	AS (Total)
ABA, n=21	Pre-intervention	4.55 ± 2.70	3.15 ± 3.08	7.33 ± 5.22
	Post-intervention	2.81 ± 2.56	2.52 ± 2.60	5.33 ± 3.95
	Δ	-1.74	-0.626	-2
	Δ%	-38.24 %	-19.87 %	-27.27 %
	P-value	0.0081	0.3506	0.0513
	Cohen's d	0.68	0.23	0.44
CON, n=22	Pre-intervention	4.26 ± 3.07	3.29 ± 2.26	6.83 ± 4.53
	Post-Intervention	2.18 ± 2.65	3.45 ± 3.62	5.64 ± 5.60
	Δ	-2.08	0.17	-1.20
	Δ%	-48.82 %	5.02 %	-17.52 %
	P-value	0.0131	0.6170	0.4571
	Cohen's d	0.74	0.05	0.24

Generally, there was a reduction of anxiety score in both abacus and control group which include all tested prescan, math and total anxiety score, except for the math anxiety score of the control group.

There were also significant reductions on the prescan anxiety score in both abacus ($p=0.0081$, Cohen's $d=0.68$) and control group ($p=0.0131$, Cohen's $d=0.74$).

Neuroimage

fMRI: Pre-training data suggested bilateral prefrontal activation during the SSA task, specifically activation over bilateral insular cortices were shown. Post-training data showed similar regional results, and the abacus training group showed increased parietal activation (Table 7). However, when 2-sample paired t-test was performed to verify this change, no significance was found (Fig. 3).

rs-fMRI-FC: Functional connectivity analysis of the resting state data showed fairly similar connection network among specific fronto-parietal ROIs. Paired t-test of the ABA group revealed increased connectivity between left Broca area and inferior parietal lobe after AMC training intervention (Fig. 4, Table 8).

Table 6. Significant prefrontal activations during BOLD serial addition task in the pilot study pre-AMC training intervention

Anatomical location				Statistical values		
Region	x	y	z	Cluster size	t-Value	p-Value
Left fronto-insular cortex	-30	21	3	78	5.72	< 0.001
Left Broca area	-39	24	15			
Left inferior frontal gyrus	-42	6	30	11	4.34	< 0.001

Table 7. Significant activations of the prefrontal-prefrontal- parasyllvian network during BOLD serial addition task in ABA and CON groups before and after AMC training invention.

Criteria	Statistical values			Anatomical location			
	Cluster size	t-Value	p-Value	x	y	z	Region
ABA pre	29	5.10	< 0.001	33	15	9	Right insular cortex
	15	4.34	< 0.001	-33	12	6	Left fronto-insular cortex
ABA post	21	7.82	< 0.001	27	-36	6	Right inferior parietal lobe
	30	6.61	< 0.001	18	9	36	Right insular cortex
CON pre	31	6.37	< 0.001	-18	-42	-15	Left inferior parietal lobe
	54	6.74	< 0.001	27	15	12	Right insular cortex
CON post	61	5.86	< 0.001	3	18	62	Bilateral medial frontal gyrus
	13	5.30	< 0.001	-34	-45	6	Left inferior parietal lobe
CON post	12	5.10	< 0.001	-33	21	6	Left fronto-insular cortex
	23	7.64	< 0.001	-39	12	6	Left Broca area
CON post	35	6.40	< 0.001	-15	6	18	Left fronto-insular cortex
	26	5.43	< 0.001	15	12	24	Right insular cortex
CON post	20	5.37	< 0.001	-12	12	45	Left medial frontal gyrus

The MNI coordinates and t-values correspond to the local maxima of the voxel clusters. The statistical threshold was set at $p < 0.005$ using Alphasim correction (with combination of threshold of $p < 0.001$ and minimum cluster size of 12 voxels) for the ABA group pre-intervention, $p < 0.05$ using FDR correction for the others.

Table 8. Significant clusters of the two-sample paired T-test within the ABA group before and after AMC training intervention

Anatomical location				Statistical values		
Region	x	y	z	Cluster size	t-Value	p-Value
Left inferior parietal lobule	-60	-36	33	124	6.10	<0.001
	-60	-30	15		5.45	
	-57	-36	21		5.26	
Right inferior parietal lobule	63	-33	36	38	4.85	<0.001

The functional connectivity seed was placed at the left Broca area ($x=-39$, $y=24$, $z=15$, radius = 5 mm). The MNI coordinates and t-values correspond to the local maxima of the centers of voxel clusters. The statistical threshold was set at $p < 0.05$ using AlphaSim correction (with combination of threshold of $p < 0.001$ and minimum cluster size of 12 voxels).

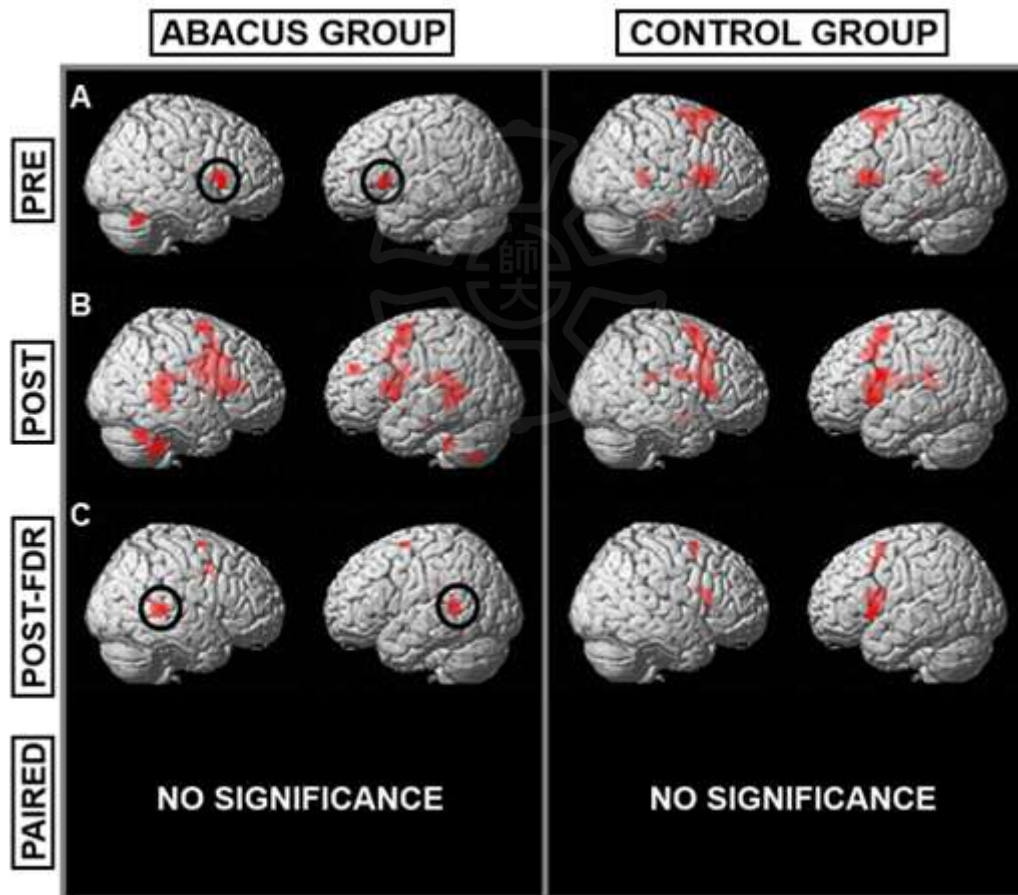


Figure 3. General pattern of activity during the serial addition task for ABA and CON groups. (A) Pre-intervention activity is mainly in the prefrontal region. (B) A general increase in post-intervention activity can be found. (C) When the within group analysis is performed with FDR correction, a shift in post-intervention activation to the parietal regions is suggested in the ABA group. However, no significance is found when two-sample paired t-test is performed. The

statistical threshold was set up at $p < 0.05$ using AlphaSim correction (with combination of threshold of $p < 0.001$ and minimum cluster size of 12 voxels) and set at $p < 0.05$ using FDR correction.

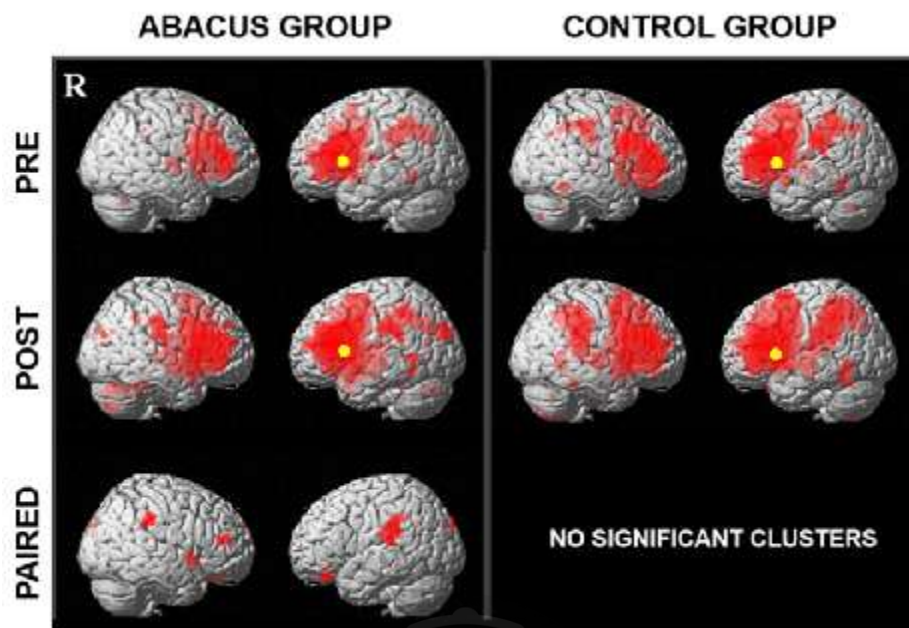


Figure 4. Resting state functional connectivity findings. The pattern of significant positive correlations between the Broca area seed ($x=-39$, $y=24$, $x=15$, radius=5 mm) and the fronto-parietal network is seen in both the ABA and CON groups. Significance in two-sample paired t-test indicates increased functional connectivity between LBA and bilateral inferior parietal lobules in the ABA group after AMC training intervention. The statistical threshold was set up $p < 0.05$ FWE correction for the within group analyses and using AlphaSim correction (with combination of threshold $p < 0.001$ and minimum cluster size of 12 voxels) for the two sample paired t-test.

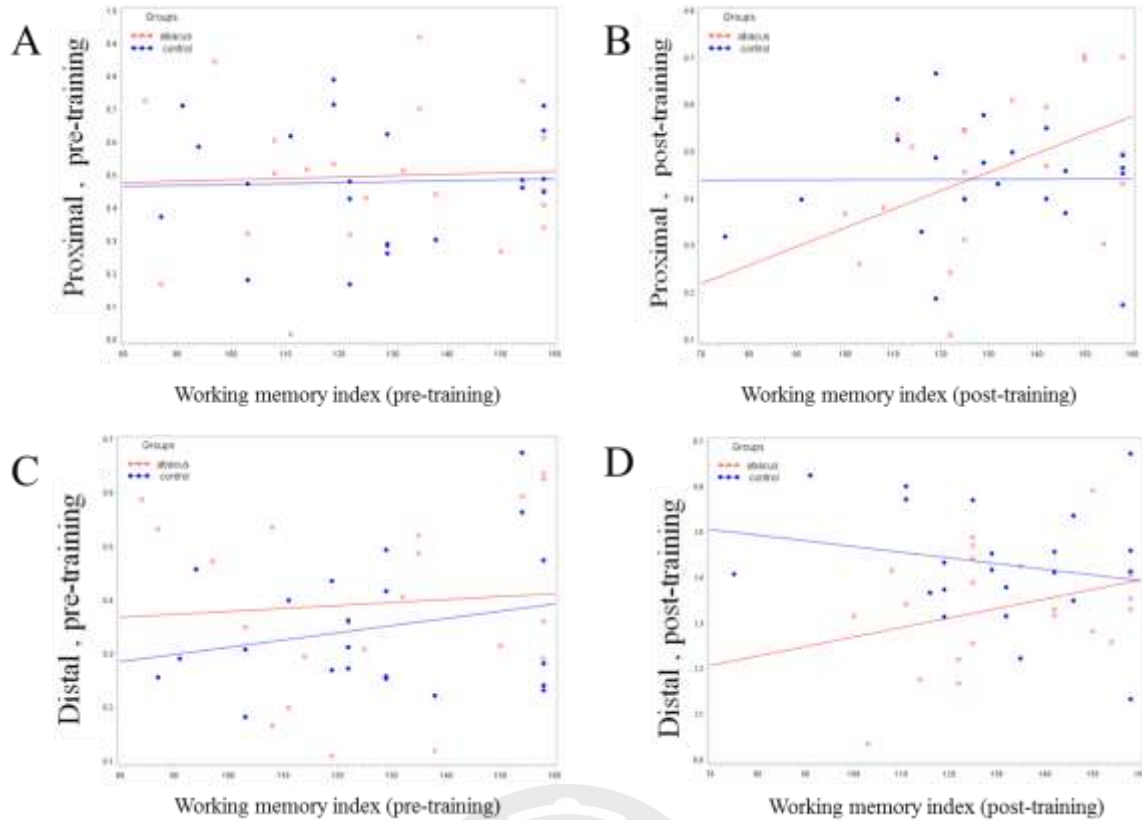


Figure 5. Correlations of functional connectivity and working memory index.

Scatterplots show the relationship between working memory scores and functional connectivity of left Broca area with two different cortical areas, both for the abacus and control groups.

The vertical axis measures the values of functional connectivity, and the horizontal axis represents the raw scores of working memory index. Proximal (pre-training and post-training) represents functional connectivity between left Broca area and left inferior frontal gyrus. Distal (pre-training and post-training) represents functional connectivity between left Broca area and left angular gyrus.

(A and C) Functional connectivity of pre-training groups did not correlate with working memory performance.

(B) In post-training abacus group, correlation between working memory index and functional connectivity of left Broca area and left inferior frontal gyrus [$n = 21$, $r(19) = 0.386$, $p = 0.069$] trended toward significance.

(D) There is a significant correlation between working memory index and functional connectivity of left Broca area and left angular gyrus [$n = 21$, $r(19) = 0.429$, $p = 0.041$] in post-training abacus group.

Table 9. Correlations between functional connectivity and working memory index

Functional connectivity	WMI, ABA group		WMI, CON group	
	Coefficient	P-value	Coefficient	P-value
Proximal-Pre training (max)	0.085	0.666	0.135	0.502
Proximal-Post training (max)	0.386	0.069	0.038	0.849
Distal-Pre training (max)	-0.019	0.925	0.281	0.156
Distal-Post training (max)	0.429	0.041	-0.249	0.201

Functional connectivity of left broca area and left inferior frontal gyrus (proximal).

Functional connectivity of left broca area and left angular gyrus (distal).

In the abacus group there was a significant increase of correlation between working memory index and post-training functional connectivity of left Broca area and left angular gyrus (distal) (Table 1). It increased from ($n = 21$, $r(19) = -0.019$, $p = 0.925$) to ($n = 21$, $r(19) = 0.429$, $p = 0.041$).

The correlation between working memory index and functional connectivity of left Broca area and left inferior frontal gyrus (proximal) in post-training abacus group also trended toward significance (Table 1) from ($n = 21$, $r(19) = 0.085$, $p = 0.666$) to ($n = 21$, $r(19) = 0.386$, $p = 0.069$). Comparatively, the control group revealed limited to no change in correlation between functional connectivity and working memory index after intervention.

Discussion

The goals of our study are as following: (1) to evaluate the relatively short term effect of six-months abacus-based mental calculation (AMC) training on the functional connectivity network, and (2) to prove the possibility of AMC training effect transfer to the untrained working memory task.

In the past decade, several reports of training on AMC have demonstrated distinct brain activations differences between experts and novices (2-5). All of the abacus-related reports are cross-sectional designs. On functional MRI results, non-experts show activity in the prefrontal and perisylvian areas, while experts with long-term training show more activation over premotor and superior parietal regions.

In recent years, structural and functional connectivity were deployed to study brain intrinsic integrity in children with 3-year training of the AMC (7,13). Increased integrity in white matter

tracts were observed over right premotor cortex, corpus callosum, and left occipito-temporal junction. The findings also suggested long-term abacus training may improve working memory capacity (7). Resting state MRI (rsMRI) revealed enhanced connectivity between right supplementary motor area (SMA), and right inferior frontal gyrus (IFG), suggesting more extensive engagement of visuo-spatial-attention networks in trained subjects while performing numerical working memory task (13). Multiple cortices on functional MRI were involved, including IFG, SMA, posterior superior parietal gyrus (PSP), and superior occipital gyrus, and it implied the long-term abacus training effects could be transferred to the untrained working memory task.

Most past studies focus on cross-sectional analysis of abacus experts and non-experts, but neglect the potential midway paradigm shift (*paradigm drift*) within the relatively long time required to become an expert. But, how soon can we expect changes after initializing training on the functional level and the behavioral level? The Chinese Abacus Association in Taiwan states that in past experience, the initial greatest level of behavioral improvement can be expected in training periods between six months to one year, implying functional changes may be in place before physical changes become detectable. Our current study seems to corroborate the aforementioned the self-evident observation in terms of brain functionality and connectivity. Stigler's study in 1986 revealed children after one year AMC training could develop the ability of mental abacus (14). Irwing's report in 2008 suggested a general intelligence improvement after receiving only 34 weeks of abacus training (6). Therefore, we assume that 6 months is the minimum period required for the change.

In present study, a uniquely longitudinal study was deployed, and we hypothesized significant changes in visuo-motor and visuo-spatial regional (fronto-parietal) functional connectivity and working memory behavioral expression within a six-month abacus training period. The WISC-IV exam's working memory subsection was used to examine the trained subjects' working memory capabilities, and to evaluate the possibility of transfer of AMC training effect. After deploying a longitudinal study, utilizing standardized behavioral tests, functional MRI, and resting state MRI, we evaluate the validity and scale of this potential change on both the behavioral level and the functional level under a relatively short-term training curriculum.

Elaboration of results

Behaviorally, the ABA group children exhibited significant improvement in working memory test after training, comparing to no improvement in control group, and showed significantly decreased reaction time when presented with the serial addition task. Younger subjects showed stronger advances in digit span and letter-number sequencing, as well as greater overall working memory competency improvement. Subjects who performed more poorly on pre-intervention tests experienced significantly stronger improvement in the letter-number sequencing subtest, arithmetic subtest, and overall working memory placement as a whole. Additionally, the ABA group children expressed a decrease in anxiety towards arithmetic processing.

On the functional level, the ABA group expressed stronger activations post-training, and within-group analysis confirms our hypothesis of a partial paradigm shift (paradigm drift) of activation zones to the inferior parietal region. Functional connectivity analysis revealed increased connectivity between the left Broca area (LBA) and the inferior parietal lobe. Association between behavioral expression and neuroimages showed increased correlation between LBA-LIFG connectivity and working memory grading after training, and LBA-LAG connectivity increases greatly in correlation to working memory grading.

Our results demonstrated improvements on both neuroimages and behavioral level could be observed in a relative short term (6 months) intervention, compared to the necessary training time to become an expert or experienced practitioner of AMC. Furthermore, the AMC training effect can be generalized to the untrained task, the WISC-IV exam's working memory subsection.

What the nature of AMC training entails?

Traditionally, abacus training was taken as a training of mental calculation, focusing on both computation speed and accuracy. AMC training in Taiwan is also a step-by-step process and its learning can be described through three stages of advancement.

Stages of AMC training:

- i. The stage of basic abacus operation (1~3 months): Oral formulas and principles of beads movement were given by instructors, and actual abacus operation was practiced repeatedly. Thus, the mental model of calculation with an abacus physical aide is introduced gradually. The operator usually become acquainted with and experienced with the physical operation within the initial three months.
- ii. The stage of beginner mental abacus (6~12 months): "Beginners at mental abacus calculation move their fingers in the air to aid in moving the mentally imaged beads."¹⁴ Intermediate operators are highly reliant on motor movements of fingers to aid in mental calculation, and the limitation of motor movements or oral distractions greatly affect the response accuracy¹⁵. Within timely practice, operators become able to add and subtract without the instrument, but the size of their mental abacus is limited¹⁶. Children usually reach this stage after about 6-12 months of training. Paper abacus?
- iii. The stage of advanced mental abacus (≥ 12 months): As they progress, experienced operators are able to perform mental calculations by imaginary movements of beads. The operation is exactly as they would do on a real abacus, involving only visual representation without physical or motor assistance¹⁵. This progress can usually be seen after one year of training¹⁴.

After the student is experienced in the practice of a mental abacus without motor aide, the series size of computation and number of digits are gradually increased. Eventually, abacus experts

become capable of executing extraordinary volumes of computation with great accuracy in compressed time.

Traditionally, AMC training is viewed as a training of mental calculation, focused on computation speed and accuracy, but a glance at the steps of learning and performance progression of AMC operators and a modern knowledge of cognitive functions show the training scheme as focused on two main abilities, the initial a visuo-motor coding scheme for transforming numbers into images of beads (17), then the visuo-spatial ability focused on proceduralizing and expanding the operator's memory span.

Simply put, memory span is increased gradually during the progress of AMC training. Thus, AMC should be viewed as a unique method of working memory training, and its operation process involves greatly with visuo-motor and visuo-spatial ability.

Paradigm drift in mental calculation after abacus training

In the local Chinese and Japanese cultural background, speed and accuracy of mental calculation is crucial to daily life and an important aspect of academic success. The “number sense” greatly depends on the parietal, prefrontal, and cingulate areas, with the HIPS playing a key part in the manipulation of quantity (18). Neuroimaging studies revealed the activation of different neural pathways between untrained children mental calculation and trained experts: the mental calculation task in children mainly activate prefrontal and perisylvian zones of the left hemisphere, with differences shown while performing simple and complex calculation; in sharp contrast, when children are trained in AMC, the activation shifts focus to visuo-motor and visuo-spatial pathways. This is consistent with our knowledge of how AMC is trained in its steps: with each cognitive focus, a change in the underlying functional network can be witnessed in the end results.

With knowledge of the training methods and its end result reflected in neuroimaging, we ask ourselves: what changes can be expected in the relatively short-term training of six months? Research show functional differences between three-year experts and untrained subjects, physical properties can be expected to change after long-term training, and general improvements are noted in time as short as thirty-four weeks. But the greatest behavioral improvements are suggested within six months to one year of training, and we proposed the intrinsic functional circuits should rightfully reflect this change.

Past studies suggest a shift of activation from frontal lobes to parietal lobes was observed with the gain of arithmetic competence, and intra-parietal shift of activation from HIPS to angular gyrus were also reported (19). Evidence for developmental change in mental arithmetic revealed a shift of activations with ages from prefrontal cortex to left inferior parietal lobe. The increased functional specialization of left inferior parietal cortex in mental arithmetic was accompanied by decreased dependence on memory and attention resources with development (20).

Our results demonstrated shift in activation region consistent with our expectation along the fronto-parietal network, but not to the extent of further parietal regions, such as angular gyrus

and posterior superior parietal cortex, as suggested by studies involving long-term trained experts. We propose the current and eventual changes to follow a paradigm “*drift*” along the circuitry, beginning at the prefrontal sectors and moving gradually to the parietal. An increase in functional connectivity between LBA and the left inferior parietal gyrus shown in our resting-state MRI results suggest the circuitry of attention improves after AMC training.

Our results also revealed a midpoint for this eventual shift that may provide deeper understanding into AMC training’s effect on the learning brain. But, what is the possible direction of future paradigm shift? PSP was proposed to be recruited for mental abacus (3,4), and the activations in angular gyrus increased with the gain of arithmetic knowledge (19). Therefore, we propose two different directions for end-term change: to shift cranially towards the horizontal intra-parietal sulcus (HIPS) and the posterior superior parietal region, or to shift dorsally towards the angular gyrus.

Working memory training and transfer

Working memory (WM) is one’s ability to keep limited information in queue and able to be manipulated over a short period of time. This specific cognitive ability is of crucial importance in many different cognitive skills or tasks, and improvement of WM capacity has been proven in several studies (8,21,22,23). WM training-related changes on brain activation were observed in frontal, parietal cortex and basal ganglia (21,22), and it was even proposed intrinsic brain activity and connectivity can be altered by cognitive training (8).

Improvement of implicit WM training can always be expected based on the repetitive training and adjustments of tasks. It is more important to evaluate the potential transfer of WM training to other non-trained tasks. The generalization of WM training effects to other non-trained tasks has been difficult (24,25), but there are promising studies demonstrating transfer after WM training to non-trained tasks can be achievable (22,23,26,27). In the current study, we rediscover a key element of Chinese culture, evaluate the validity and effectiveness of AMC training as a tool to augment WM capacity, and verify the possibility of training effect transfer to the untrained working memory test.

AMC is a relatively complex activity, and requires longer-term training in comparison to conventional WM training regimes. However, it also involves multiple cortices in its training, providing a higher transfer potential to untrained tasks, a key factor in the choice of curriculum. Past WM training regimes are task repetition-focused; in contrast, AMC training implements a non-task-specific model that is more attractive to young neophyte subjects. It is a natural way of improving WM capacity, and its effective educational methods have been honed culturally over time to become a subject of its own.

Of course, despite all its pros, AMC training is far from perfect. It has its share of limitations one must consider before engaging. Firstly, the *number sense*, understood in mathematics education as “an intuitive understanding of numbers, their magnitude, relationships, and how they are affected by operations,” should be intact before the subject initiates training. In general

curriculum, this would require children of at least eight years of age receiving public education, as youths under this age would not have the math cognitive capacity to manipulate numbers at a level suitable for the AMC model. Secondly, the initiation of AMC training focuses on reinforcing the number sense of subjects and introducing the abacus model, the latter steps exercise the visuo-motor and visuo-spatial networks and eventually zooms in on increasing the memory span with a practiced paradigm. This scheme is a very time-consuming process and requires a significant amount of attention. When considering AMC as an option for WM training, the minimum training time length for substantial effect and subject interest should be considered. Lastly, after an extended time of training, diminishing returns can begin to occur in regards to the AMC training effect on WM as a result of over-learning. Studies suggest after over-learning, the abacus operator requires only a limited amount of attention for the calculation task and is significantly less stimulated by the operation, only exercising a practiced model (15). We advise the use of AMC training as a WM exercise to be limited to one to two years, when the effects on WM capacity are most significant and time-efficient. Alternative training regimens of a more creative nature should be considered after the initial mental abacus model is practiced for a more interesting approach and greater benefits to the learning subject. These limitations, under closer examination, are present in most, if not all WM training regimens, but AMC training provides a more comprehensive and tolerant range.

The effects of training in brain plasticity are undeniable, but the future focus should be for which training regimens may result in the best transfer effects, and to whom it is most beneficial (23). AMC training can be considered as an effective method of WM training with a time constraint. Despite its limitations and time-consuming training regimen, it provides stronger training results and retains higher transfer potential than conventional WM training. In modern era, with calculators that can be operated by the simplest of minds, we propose to view the abacus no longer as a tool for trade or computation, but as a toy to learn through play.

Potential cultural and educational impacts

Abacus training is a culturally unique experience that enters the lives of Chinese children to varying degrees, and its training effect of speeded mental calculation is considered to be essential to success in mathematics. Stigler describes in his 1986 document the training took place during the fourth year of primary school in Taiwan (14), but the practice has fallen out of public education in recent years, and is currently replaced with a general arithmetic curriculum. Now it is regarded as an extracurricular activity only pursued by those specifically interested in mathematics deftness and focus. In review, it should be taken as an interesting and prospective method of brain-based education which allows the learner to practice arithmetic operation and also train working memory through activity. With its benefits in mind, educators should review the viability of AMC training in primary education curriculum.

Conclusions

Within the relatively short (6 months) training of abacus-based mental calculation, significant changes were observed in fronto-parietal network and working memory behavioral expression. Functional connectivity analysis with rsMRI revealed increased connectivity between the left inferior frontal area and the inferior parietal lobe. Most importantly, the AMC training effect can be generalized to affect the untrained tasks of the WISC-IV exam's working memory subsection. But are these effects persistent in the long run? And furthermore, what is the required amount of training before one completes the paradigm shift to “transform” into the mental model as that of experts? And even though the present study shows AMC training effects generalized to untrained working memory tasks, but there is still a long way to go before the leap is made to complex cognitive abilities such as reading, arithmetic, or general intelligence. We recommend future AMC-related studies place focus on the training conditions and target subjects most suitable to produce lasting effects on the mental scheme. Additionally, the evaluation of transfer effects should not be to general skill assessments involving multiple complex cognitive abilities but to specific cognitive traits.

In conclusion, this study offers reappraisal of the abacus, a traditional Chinese tool, and its training in the modern setting. Compared to the common practice of task repetition, AMC training is a more complex and interesting method of cognitive training with a stronger sense of self-accomplishment through its step-by-step training curriculum. Our results also suggested AMC training may increase learners' confidence in arithmetic tasks and alleviate anxiety. It has potentially long-term positive psychological effects in future learning. AMC is not only an arithmetic operation, but it is also an appropriate tool to improve working memory capabilities by exercising visuo-motor and visuo-spatial skills. With aid of educational neuroscience, we can take a new perspective on the traditional Chinese tool for not only calculation but also learning in the modern age.

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Appendix

Oral papers 01

■ The Design of New Teaching Model of Neuroanatomy to Prevent Neurophobia in Preclinical Medical Students.

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99 年 11 月 6 日 台北醫學大學 台北

Background:

Neurophobia, being described as “a fear of the clinical neurosciences”, is a longstanding problem among preclinical medical students. The lack of knowledge in the complexity of neuroanatomy is regarded as one of the most important reasons. Therefore, a new teaching model of neuroanatomy was developed.

Summary of work:

We combined traditional method and contemporary virtual reality technologies to design this new teaching model of neuroanatomy, including anatomical atlas sketch, pretest and posttest of reading brain computed tomography scans, and teaching with dextroscope.

During July 2009 and July 2010, fifty-five medical students in Taipei Medical University Hospital were enrolled in our study.

Summary of results:

The significant improvement between the mean scores of pretest and posttest was observed.

Questionnaire results revealed that most of the students express strong positive attitude toward learning in dextroscope, and the teaching model of neuroanatomy. Moreover, they also showed more confidence on learning neuroanatomy after being taught with dextroscope.

Conclusion:

A carefully designed teaching model of neuroanatomy could possibly help medical students to overcome neurophobia. Besides, dextroscope is a friendly learning environment of virtual reality.

Take-home messages:

The traditional method of teaching neuroanatomy could be integrated with new virtual reality technologies to innovate a curriculum of the future.

Introduction

Anatomy has been the fundamental medical knowledge for centuries since renaissance, but the teaching of anatomy is facing significant challenges in recent years. A great leap in the development of digital medical images has provided new ways to see through the structure of the human body. With the rapid advances in information technology, the role of diagnostic radiography in anatomy education is expanding [1]. Many reports had pointed out the potential roles of digital medical images to enhance the teaching and learning of anatomy [1,2].

However, there is a developing debate on methods of teaching anatomy. The use of cadaver dissection is still a traditional and important part in the Anatomy course for medical students. But, could it be totally replaced by computerized anatomy resources, (including diverse software and websites)?

Rapid evolution of three-dimensional images technologies has made virtual environments (VEs) possible in recent years. The applications of virtual reality (VR) on health care are diverse, including surgical planning and simulation, medical education, patient simulator, psychological assessment, rehabilitation, bronchoscopy, et al [4]. The applications of virtual reality (VR) in surgery include anatomy education, preoperative planning and simulation, and assessment of surgical skills.

The results of applications of VR techniques in preoperative planning and simulation are promising, especially for laparoscopic surgery and neurosurgery [4,5,6]. The task performance in simulator is strongly correlated to daily surgical performance [7]. The implementation of VR in anatomy education also has great potential, but could it influence the learning of reading skills of diagnostic images for medical students?

Moreover, the role of virtual reality (VR) in the teaching of anatomy is revolutionary and with great potential [3,4]. Since the Visible Human Project (VHP) launched by the US National Library of Medicine in 1988[11], it allowed the developments of various VR 3-D models. The most renown is the Visible Human 3D Anatomical Structure Viewer (EPA Lausanne) [12].

3-D visualization of clinical diagnostic images allows a deeper understanding of spatial relationships between deep structures that hardly can be achieved by other teaching methods [4]. Taking brain neuroanatomy as an example, trainees thus can see the sophisticated and delicate neural structures by dynamic dissections from various directions with the help of VR.

VR definitely improve the learning of anatomy. But, could the VR techniques influence the learning of reading skills of radiological anatomy (diagnostic images) for medical students?

Radiological anatomy is totally different from gross anatomy. Medical images are another representation of gross anatomy, and anatomy knowledge gathered from dissections always needs being translated into cross-sectional views of clinical images [11]. That is why students often feel frustrated while reading cross-sectional clinical images (such as, brain computed tomography scans) at the first moment.

Therefore, appropriate learning scaffolds are needed as the bridges of knowledge among those different representations of anatomy.

The learning of reading brain computed tomography (CT) scans is a critical step in studying clinical neuroscience, but it seems to be a major obstacle to medical students. The most difficult parts are lack of the acquaintance of medical terms and 3-D concepts of neuroanatomy.

Therefore, we are developing a new model of teaching clinical neuroanatomy for preclinical medical students. The teaching model includes sketch of atlas of neuroanatomy, self-directed learning of reading brain computed tomography (CT) scans, and implement of dextroscope. We are in the hope to teach gross anatomy in the context of clinical setting.

Sketch is an unique skill commonly used in medicine, and it is especially important in the training of surgery. Students have to recognize what structures they are going to sketch, and allocate them in a proper position after knowing the spatial relationship between neural structures. Sketch could help students to recall the unfamiliar and difficult neuroanatomical terms, and restructures 3-D concepts of neuroanatomy inside students' minds.

Dextroscope (Volume Interactions, Ltd., Singapore) is a virtual reality system for preoperative planning and simulation of surgery. Patient-oriented and fused medical images are presented stereoscopically and the fused images can be manipulated freely from various dimensions. Some degree of simulation of bone drilling and brain retraction can be implemented in the dextroscope. With the help of dextroscope, students can trace vascular and neural structures in dynamic serial images, and further establish a deep understanding of the spatial relationships between individual structures.

This new model of teaching clinical neuroanatomy definitely encourage students to learn clinical neuroanatomy in a more interesting and promising way. However, we also want to see if we could improve the learning of reading skills of brain computed tomography (CT) scans with the help of dextroscope? Part of the aim of our study is to see if VR can improve students' confidence of reading brain CT scans.

What is Neurophobia?

Neurophobia is described as “ the fear of clinical neurosciences ”. It is a worldwide phenomenon among medical students[13].

Neurological diseases is becoming more and more popular. Brain computed tomography (CT) scans gave become a regular and screening scans for diagnosing neurological problems. Learning to read brain CT scans is the crucial first step to learn clinical neurosciences.

However, atlas in anatomical textbooks and brain CT images are different representations of neural structures. Medical Students' memory battery for neuroanatomy is very poor. Students have difficulty to have far transfer of anatomical knowledge, which was learned years ago.

Therefore, an integrated program is needed to path the ways for the learning of basic and radiological neuroanatomy. The aim of this study was to evaluate the impact of dextroscope on

the learning of radiological neuroanatomy, and to verify that if virtual reality simulator, dextroscope, could help the learning of reading brain computed tomography scans.

Methods

Sixty-five preclinical medical students in Taipei Medical University Hospital were enrolled in this study. All of the successive students rotate in the department of neurosurgery for two weeks, and they are divided into two groups. The implement of dextroscope is used as a treatment for the students of the group one.

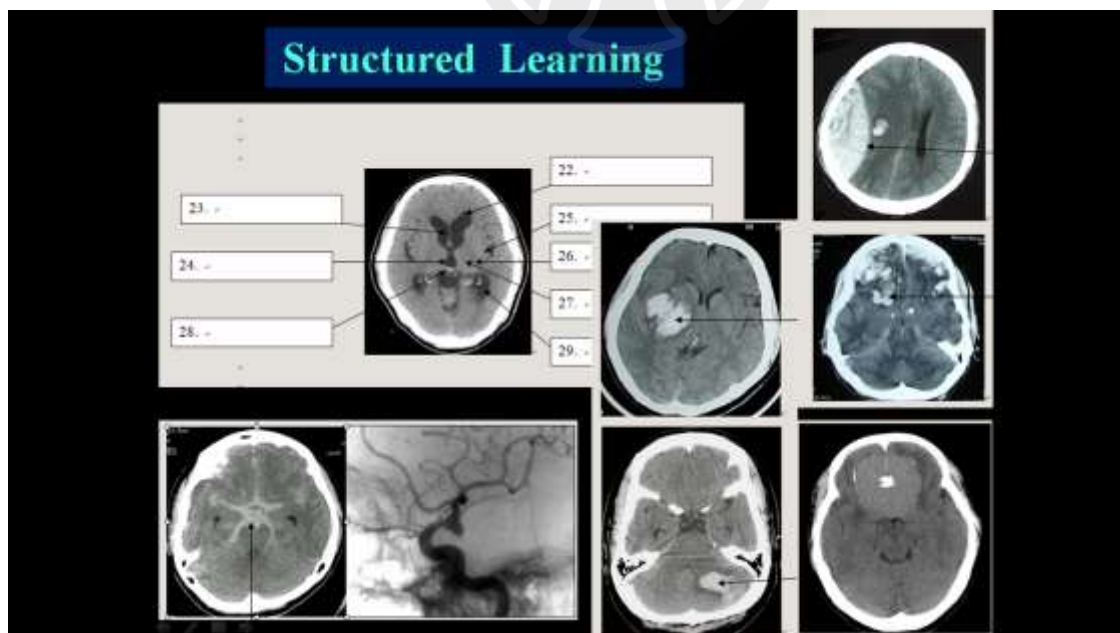
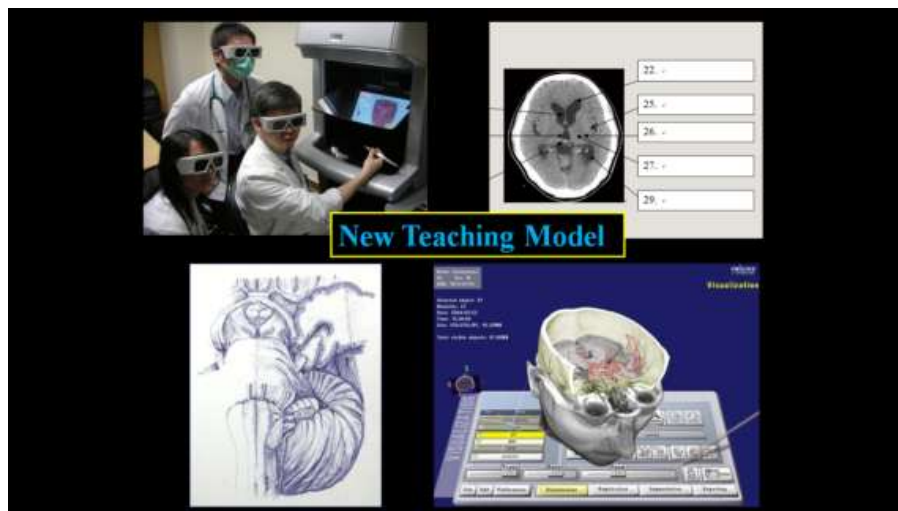
Thirty-five students are in the group one, and the timetable of teaching activities is as the following. On day1, and day 2 of the rotation, students are asked to sketch atlas of basal ganglia and brain stem, and the terms of neuroanatomy structures will be indicated. Then they need to complete a self-study brain CT scans test (including fifty questions), as the pretest, during the first week rotation, and their answers will be discussed with teacher on the 8th day. Dextroscope will be taught for one hour on day 5 and another hour on day 13 of the rotation. The post-test of brain CT scans is held on day 13 after the teaching of dextroscope finished.

Thirty students are in the group two, and the timetable of teaching activities is as the following. On day1, and day 2 of the rotation, students are asked to sketch atlas of basal ganglia and brain stem, and the terms of neuroanatomy structures will be indicated. Then they need to complete a self-study brain CT scans test (including 50 questions), as the pretest, during the first week rotation, and their answers will be discussed with teacher on the 8th day. The post-test of brain CT scans is held on day 13. Dextroscope will be taught for one hour, as salvage instruction, only after the post-test of brain CT scans being finished.

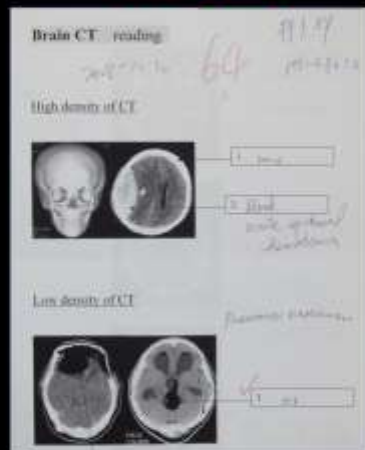
Learning attitude questionnaire and self-confidence questionnaire are completed after the rotation. Degree of satisfaction is divided into five grades.

The fifty questions of pretest of brain CT scans include thirty questions of neuroanatomy and twenty basic clinical questions. Full score of the fifty questions is one hundred.

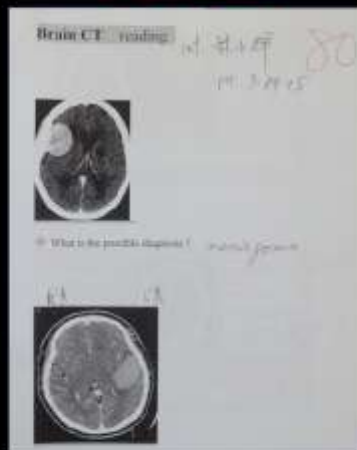
The composition of the fifty post-test questions is slightly different from the pretest's. Seven advanced clinical questions are added, and they are deployed to indicate the problem-solving ability of students. Therefore, the fifty post-test questions are composed of twenty-six questions of neuroanatomy, seventeen basic clinical questions, and seven advanced clinical questions. Full score of the post-test is also one hundred.



Pre-test



Post-test



Results

Table 1. Results of sixty-five students.

	Mean	SD	Rate of correct Answers
Pre-test	71.29	8.4	Full mark : 100
Post-test	89.91	6.3	
Clin. A (7tests)	8.46	2.42	60%
Clin. B (17tests)	31.94	2.74	94%
Anat. (26tests)	49.24	3.47	95%

E.S. (Cohen's D): 2.53 : huge effect size.

Table 2. Results of different groups.

	Treatment	Pretest score	Post-test score	Score Increment
Group one	With Dextroscope (35 students)	71.9	90.0	18.1
Group two	Without Dextroscope (30 students)	66.8	87.9	21.0

Discussion

Besides cadavers and dissecting room, there are emerging methods of teaching gross anatomy with the generalization and advance of computer technology [1,2,3,4]. But, could cadaver dissection be totally replaced by computerized anatomy resources? Biasutto et al. (2006) argued that there were no objective and scientific data to prove the superiority of computerized resources over cadaver dissection, and demonstrated that the best way of teaching anatomy is the combination of cadaver dissection and computerized materials [2].

There are three major applications of virtual reality (VR) on health care: anatomy education, simulation of operation, and radiology education.

The application of virtual reality (VR) has led anatomy education into different horizon [3,4,7]. Through interactive 3-D graphics, students can explore internal structures in various dimensions. Anatomical structures are represented in dynamic images, and it allows trainees to trace all kinds of tissues from multiple viewpoints [4]. Therefore, students can attain a deeper understanding of spatial relationships between different structures that cannot be achieved by other teaching methods.

The simulation of operation in virtual reality (VR) environments has been introduced successfully in recent years, especially in laparoscopic surgery and neurosurgery [4,5,6,8,9,10]. With the advances of endovascular techniques and radiosurgery, there are more alternative methods of treating cerebral aneurysms or skull base tumors. The decrease of open operative cases is making young neurosurgeons more difficult to develop their surgical skills [8]. VR technologies provide a no-risk environment for preoperative rehearsal, and it allows residents to simulate operation preoperatively. Therefore, neurosurgeon can somehow keep experienced in those rare and complicated surgeries with the implement of VR technologies.

Nonetheless, virtual reality is never like actual surgery. It allows some degree of rehearsal of bone drilling, brain retraction, and simulation of possible trajectory and probable difficulties encountered during operation. However, all of this advantages are the initial steps of performing surgery. In real life, the unpredictability during actual operation is more challenging. The experience in computerized simulator could not offer similar tactile and emotional training from the real world experience.

Significant progresses in medical imaging in recent years have enhanced the potential role of radiology over anatomy education. Since the introduction of Visible Human Project (VHP) by National Library of Medicine (NLM) in 1988[11], digital diagnostic images can be processed in various ways. Medical images are restructured in 3D style, and it has made virtual reality resources available for radiology education. Students now can see the structures in a more comprehensive way, and spatial relationships between structures could be realized nearly without any limitation. But, could the VR techniques improve the learning of reading skills of clinical images, ex. brain CT scans, for trainees?

The design of our new teaching model for neuroanatomy adopted sketch (the traditional learning method) and dextroscope (VR technology) to facilitate students' learning of reading brain CT scans. From our preliminary results, there are no differences of average marks and improvement between study and control group. The treatment for this teaching model, dextroscope, seems to have no role on the learning of reading brain CT scans. However, based on the primitive results of the learning attitude questionnaire and self-confidence questionnaire, students do feel direct help and deeper understanding of spatial relationships between structures from the teaching of dextroscope, and they also show more confidences on the following learning of clinical neuroscience.

The significant improvement between the mean scores of pretest and posttest was observed. Questionnaire results revealed that most of the students express strong positive attitude toward learning in dextroscope, and the teaching model of neuroanatomy. Moreover, they also showed more confidence on learning neuroanatomy after being taught with dextroscope.

Conclusion

Our new teaching model for neuroanatomy seems to enhance the learning of reading brain CT scans. A carefully designed teaching model of neuroanatomy could possibly help medical students to overcome neurophobia. Besides, dextroscope is a friendly learning environment of virtual reality. Therefore, the traditional method of teaching neuroanatomy could be integrated with new virtual reality technologies to innovate a curriculum of the future.

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從大體解剖實驗到虛擬實境：談解剖學教學之新趨勢

鄭泳松¹ 陳建宇² 張俊彥³

摘要：人體解剖學自古以來被視為醫學知識的重要基石。過去大體解剖實驗是醫學生學習解剖知識最直接也最普遍的方法，然而隨著近年來電腦科技日新月異，放射學與數位醫學影像提供臨床醫師另一種角度來探索人體解剖構造。因此，我們提問：「以電腦科技為主之解剖學教學可否取代傳統之大體解剖實驗？」並且我們也想探究虛擬實境之教學在現今解剖教學上之功能與角色。本文回顧與分析相關文獻，嘗試能在不同的解剖學教學法上，針對醫學生學習解剖學時所面臨的困難，進而找出有效整合基礎與臨床解剖學的教學課程與內容。

關鍵詞：解剖學教學，大體解剖實驗，電腦醫學影像，臨床解剖學，虛擬實境
(台灣醫學 Formosan J Med 2015;19)

緒言

自從西元十五、十六世紀文藝復興時代以來，懷疑、探索未知、與實驗的精神當道，經由對人體直接解剖所描繪與建構出的解剖學知識，幾個世紀以來一直被奉為圭臬，大體解剖向來是學習解剖學知識最主要的來源。

大體解剖(cadaver dissection)或屍體解剖(autopsy)在疾病診斷的準確性方面亦扮演著舉足輕重的角色[1]。透過對大體或屍體的解剖與臨床病理討論會(clinical pathology conference)的進行，臨床醫師能夠回顧病人診療的過程，瞭解疾病在身體裡的具體表現，探討可能的致病機轉，檢討診斷的準確性與治療的妥切性，建立臨床診斷與治療過程的標準化，從而建立醫院健康照護的標準化流程。

因此，經由解剖大體所構建的不僅只是解剖學知識而已，更重要的是透過解剖大體所建立的臨床關聯性，促成對疾病更深入的研究與瞭解。所以，以大體解剖實驗為主體的解剖學教學在醫師的

養成教育上佔有極重大的角色與地位。

然而，近年來電腦科技不斷地快速發展，以傳統的大體解剖實驗所主導的解剖學教學方法的地位也不斷地受到挑戰。全面電腦化的醫學影像，不僅讓影像資料檔案的儲存、傳輸與轉換的方式產生劃時代的改變[2]，更重要的是，數位化的醫學影像品質更清晰，可能的應用與發展性也更廣泛，同時可以提供的解剖學教學工具也更多元化[2,3]。許多的文獻報告均指出電腦醫學影像在提升解剖學教學上佔有潛在的地位與角色[2,4]。例如，3D立體化的影像技術可以提供解剖構造更細緻與更精準的立體空間關係(spatial relationship)，而虛擬實境(virtual reality)技術在解剖學教學的應用上更是具有革命性的發展[5]。以腦部神經解剖學為例，學生藉由動態的3D立體化醫學影像解剖過程，不僅能對複雜的神經解剖構造有更3D立體化的瞭解，同時也能有效地模擬真實的神經外科手術進行中可能面對的困難與挑戰，進而學習神外手術路徑(neurosurgical approach)的方法。

因此，電腦醫學影像技術的進步，不僅促進

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了臨床影像診斷的品質，同時也提供不同於以大體解剖為主的解剖學教學方法，甚而能在手術前提供外科住院醫師虛擬的3D立體手術模擬環境，達成手術模擬與手術教學的目的。

然而，在這超現代的電腦資訊革命時代裡，新興的電腦軟體解剖學教學是否能夠完全取代以傳統的大體解剖實驗主導的解剖學教學？這問題一直存有不少的爭議[3,4]。

本文因此進行相關的文獻分析，希望能針對不同的解剖學教學方法，做出進一步的研究與探討。除了教學法的討論之外，本文也希望能夠深入了解醫學生學習解剖學時面臨的困難，進而找出有效整合基礎解剖學與臨床解剖學的教學課程與內容。而這其中，更是有幾個重要的面像需要被認真地面對與討論：

一. 驟然改變所可能帶來的危險與後遺症？

在英國，有數家全新成立的醫學院，對於醫學院的課程與教學作出了劃時代的改變。其中，半島醫學院(Peninsula Medical School)於2002年9月成立後開始招生，更是創風氣之先，將大體解剖實驗完全排除於解剖課程教學之外[3]，取而代之的是PBL的課程 The four-part approach：包括有表面及活體解剖學(surface and living anatomy)、醫學影像、虛擬實境影像(virtual-reality imaging)，及臨床技能模擬器(simulator)。

「直接停掉解剖實驗教學」，在這種解剖學課程驟然改變的背後，並沒有充分的科學證據作後盾，可能隨之而來對於醫學教育的衝擊，並沒有被完整評估。如此一來，就有可能會發生無法控管的風險，例如：讓解剖知識不足的醫學生後來擔任外科醫師的工作[3]。

二. 在基礎醫學與臨床醫學之間，解剖學知識的連貫性！

在醫學領域的各個學習階段，無論是醫學生時期、見習醫師時期、實習醫師時期、或是臨床醫師時期，解剖學知識都很重要。但是，不同時期需要的內容可能完全不同。

其中，愈是重要的經典，愈需要在小時埋下種籽，雖然小和尚念經有口無心，但是一顆種籽落

地，總會發出許多種籽來。例如：神經解剖學的學習。

在筆者任職的醫學院，約莫十年前將原本是必選的神經解剖學與實驗課，改為選修課，許多學生礙於學習難度等理由，因此未選獨讀此門現代醫學極為重要的課，後續的結果便是：神經學恐懼症(Neurophobia)。因而導致高年級醫學生在學習臨床神經內外科學、或是神經影像學時，面臨極大的學習障礙。而神經學恐懼症最主要的原因就是：神經解剖學知識的缺乏與神經解剖學教學的不足。

因此，在「解剖學知識連貫性」的前提下，將不同困難程度的解剖學教學分布在醫學生的各個學習階段，如何通盤考慮？需要認真的研究與面對。

三. 臨床解剖學的重要性！

何謂臨床解剖學 (clinical anatomy)? 直接的說也就是：臨床醫學生及臨床醫師需要的解剖學。臨床醫療需要的解剖學知識主要有兩大類：外科解剖學(surgical anatomy)與放射影像解剖學(radiological anatomy) [3]。小從置放鼻胃管，置放中央靜脈導管(CVP)，閱讀醫學影像，執行醫療檢查，大到手術治療，解剖學幾乎無所不在。臨床解剖學更是臨床醫師面對病人的問題時，推理(thinking process)的基礎。因此，當務之急應是以臨床解剖學的角度，來省思解剖學的教學方法可能的改變。

四. 解剖實驗課程要如何改變？

要怎麼改變？需要智慧，需要科學證據，來帶領課程改革的方向[1]。而可能隨之而來對於醫學教育的衝擊，需要被完整評估[3]。可能的革新方向包括幾個層面：解剖學實驗課程時數與內容、解剖學實驗課程師資的組成(例如：引進臨床醫師作為師資)、與教學方式的改變。

不同立場闡述

一. 以大體解剖實驗做解剖學教學的優點

(一) 學習解剖學知識最直接、有效的方法

自從西元十五、十六世紀文藝復興時代以來，經由對人體直接解剖所描繪與建構出的解剖學知

識，幾個世紀以來一直被奉為圭臬，大體解剖向來是學習解剖學知識的主要來源。臨床醫學服務的對象是人，解剖學家相信唯有透過對人體直接做解剖，經由反覆的觀察與比較，才能獲的正確的解剖學知識。因此，大體解剖實驗是醫學生學習解剖知識最直接也最有效的方法。

(二) 建立解剖與臨床的關聯性

在二十世紀八零年代以前，疾病的正確診斷常需仰賴對屍體的解剖，透過臨床病理討論會(clinical pathology conference)的進行，臨床醫師能夠瞭解疾病在身體裡的具體表現，同時也能回顧病人診斷與治療的過程，探討可能的致病機轉，檢討診斷的準確性與治療的妥切性，促成對疾病更深入的研究與瞭解。因此，解剖大體或屍體所獲得的不僅只是解剖學知識而已，更重要的是透過對人體的解剖所建立的臨床關聯性[1]。所以，以大體解剖實驗為主體的解剖學教學在醫師的養成教育上佔有極重大的角色與地位。

(三) 有效訓練解剖結構 3D 立體空間關係

系統性解剖學知識(systemic anatomy)能夠給予學生整體的解剖學概念，就像旅行者隨身攜帶的旅遊地圖一樣，讓學生在腦海裡存有一個條理分明的解剖圖，知道組織結構的來龍去脈，而不僅只是強記的、零碎的解剖學知識。然而，臨床醫師需要的不僅是系統性解剖學知識，同時也需要區域解剖學(regional anatomy)的概念。若從臨床或外科學的觀點來看，區域解剖學概念的重要性可能常常凌駕於系統性解剖學知識之上。

大體解剖實驗提供了一個真實體驗區域解剖學概念的機會。在操作大體解剖實驗的解剖過程中，醫學生依靠著腦中的解剖學知識當引導，逐步地劃刀，切開皮膚、脂肪、神經、血管、肌肉等不同層次的組織，同時觀察、尋找、分辨可供辨識的組織結構。經由這樣的解剖訓練過程，醫學生能夠仔細徹底地了解不同的解剖構造之間相對應的 3D 立體空間關係[3]，有效建立區域解剖學的概念，以獲取臨床照護所需的解剖學知識。

(四) 慢就是快？！大體解剖實驗是外科學的基礎扎根教育

良好的體力、耐力、觀察力、情緒的控制能力、心眼手的協調性、敏銳的手部觸感，這些能力

都是外科醫師不可或缺的重要特質。大體解剖實驗就是一種外科實驗，只是解剖對象是不流血的大體。長時間待在充滿刺鼻藥水福馬林的解剖實驗室，對醫學生而言，便是體力與耐力的重要考驗。解剖的過程本身不僅是機械式的手部動作，學生在運用解剖器械時，能夠發展手部的觸感與靈活度，同時鍛鍊心、眼與手的協調性，並且在泡過福馬林的組織結構裡，仔細觀察，努力分辨出可辨識的組織構造，這樣的過程，就是基本的外科實驗過程，因此，大體解剖實驗是外科學的基礎扎根教育[1]，經由這樣的解剖實驗教育，能夠讓醫學生在從解剖學教室走向開刀房時，裝備好外科學必要的先備知識。

(五) 死亡與臨終教育的第一章 first patient

人類從哇哇墜地之後，就一路不回頭地走向死亡。因此，死亡教育是極為重要的生命教育，尤其是對未來要負起他人生命健康的醫學生而言更為重要。對大多數的醫學生而言，往往在解剖實驗室裡初次與遺體面對面(first patient)。因此，解剖實驗室是開啟死亡與臨終教育最好的教室。與遺體首次面對面這樣鮮明的體驗常常會觸發學生強烈的情緒反應，回憶起自身面對至親好友重病或瀕臨死亡的經驗，其中的苦痛、焦慮、恐懼、未知與沉思。這樣的情緒與思維無形中將解剖實驗室裡的經驗提升到類似心靈層次[1]，而如此的經驗正是解剖學科老師開啟對醫學生「醫學人文教育」最好的時刻。所以，解剖學科老師在解剖實驗室裡能夠扮演的角色，將不再只是傳統思維裡教授解剖學知識的書匠，更可以將死亡教育與人性關懷教育融入在解剖實驗課程裡，替醫學生未來的臨床醫學教育扎下一個穩固的基礎。

國內的醫學教育學者賴其萬等人更強調將人文與醫學整合在大體解剖課程裡的經驗。其報告裡指出，台灣此一新成立的醫學院以不同於以往解剖學的課程設計，將醫學人文教育融入於課程之中。讓醫學生在解剖實驗開始之前，提供大體捐贈者家屬與醫學生見面的機會，讓學生了解捐贈者生前的事蹟，並且讓學生透過追思儀式的過程，表達對捐贈者及其家屬深切的尊敬與感謝。透過對醫學生的問卷調查發現，對醫學生而言，大體並不只是「教學或學習的工具」而已，大多數醫學生覺得認識大體捐贈者的生平事蹟、解剖實驗後將大體縫合、以

及解剖結束後舉行的追思儀式，對他們非常有幫助。而且，如此的解剖學課程設計能夠幫助他們未來成為臨床醫師時，「對病人的照顧更有熱情和愛心」。

(六) 團體合作 teamwork

臨床醫療照護需要醫師、護理、醫事人員的通力合作，才能達成最佳的臨床服務。而解剖實驗能夠順利進行更是有賴實驗小組成員發揮團體合作(teamwork)的精神，才能在艱苦的解剖室裡，接棒完成解剖實驗。

二、以大體解剖實驗做解剖學教學的缺點

(一) 大體解剖後壓力症候群 post-dissection distress syndrome

大體解剖實驗課程在解剖學的學習上佔有極重要的地位，但是，解剖實驗課程也有可能使醫學生產生負面情緒或生理上的壓力。根據印度的研究指出，在第一次接觸大體時，有 47.5%的醫學生曾經有過 emotional shock 的經驗，而有 18.75%的醫學生在解剖實驗課程進行中持續懷有壓力和焦慮的感覺。另一項調查顯示，有 2%的學生不良反應持續一年。因此，如何讓學生對於接觸大體時所產生的不良反應獲得適當的引導與治療，將是進行相關實驗時不可忽略的議題。

(二) 大體保存的品質

大體解剖標本在消毒液(福馬林)的處理過程中，大體保存的品質並不容易受到嚴格的控制，經過福馬林處理的解剖標本，在外觀、顏色、人體組織的質地必定會產生不同程度的變化[3]。因此，在解剖實驗室裡所獲得的解剖經驗，(例如：觸感的訓練)與外科手術的經驗可能完全不同。

(三) 健康風險

處理解剖標本的消毒液(福馬林)可能直接帶來健康上的風險，(例如：引發氣喘或其他呼吸道的疾病)。此外，解剖標本本身亦有可能潛藏著消毒液無法滅絕的致病源，(例如：愛滋病或狂牛病)。

(四) 侷限在區域解剖學的概念 regional anatomy only

臨床醫療需要的解剖學知識主要有兩大類：外科解剖學(surgical anatomy)與放射影像解剖學(radiological anatomy)[3]。在大體解剖實驗的訓練過程中，醫學生的確能夠仔細了解不同的解剖構造

之間相對應的 3D 立體空間關係，有效建立區域解剖學(regional anatomy)的概念。

然而，臨床診斷時所需要的放射影像解剖學知識常常是切面解剖圖(cross sections)。所以，醫學生在習得區域解剖學的概念後，當在臨床醫療面臨閱讀醫學影像時，常常需要再重新將已習得的區域解剖學概念與切面解剖圖(cross-section anatomy)之間作轉換[3]。因此，經由大體解剖實驗所習得的解剖學知識有其侷限性。

(五) 不可重複性

解剖後的大體無法提供給另一組學生作為再度解剖的使用，因此不具有教材使用之可重複性。

三、以電腦醫學影像做解剖學教學的優點

(一) 較易引發學習興趣

例如在六維影像系統(dextroscope)的學習環境裡，大多數的學生會覺得像走 Discovery channel 的電視頻道裡[10]。因此，電腦化或動畫式的醫學影像，比起大體解剖實驗，較能夠有效提高醫學生的學習興趣。

(二) 解剖學知識的可親性 accessibility

網路資訊科技的快速發展，使得電腦醫學影像資料檔案的展示、傳輸與儲存有更多的方式。醫學影像系統(picture archiving and communication systems, PACS) 能夠傳輸影像資料檔案到不同地點，提供臨床與教學不同的使用[3]。例如在六維影像系統(dextroscope)裡，學生可以典藏/archive整個學習過程。提供學過的解剖知識隨時隨地複習的機會。讓醫學生能夠不受時間、空間的限制，更自如地學習想要學習的解剖學知識。

(三) 可透視的解剖學

電腦斷層CT與核磁共振MRI的發明將臨床醫學影像帶入可透視解剖學的境地。CT、MRI的發明獲得諾貝爾醫學獎，使醫學成為眼見為憑的醫學，不再瞎子摸象。探究人體內部器官的構造不再是外科手術的專利，CT和MRI可提供內部組織器官高解析度的影像，讓臨床醫師可以清楚的看見病灶與正常組織之間相對應的解剖關係。SPECT、PET和MRI等功能性影像更可以顯影出局部組織代謝時的生理變化[1,3]。同時，透過動態影像與核子醫學攝影的技術，電腦醫學影像更可以顯示內部器官的動作

影像(organ motion, 例如 the beating heart), 或者是追蹤放射線物質在身體裡代謝的途徑。因此, 醫學影像不再局限於只能提供純粹的結剖構造訊息, 更能夠顯示結剖構造與身體正常的生理功能間直接的相對應關係。

(四) 3D 立體化的解剖學

傳統的 X 光攝影僅只能顯示單一平面的二維影像(2D), 隨著電腦動畫技術的進步, 3D 立體化的電腦醫學影像技術可以提供解剖構造更細緻與更精準的立體空間關係(spatial relationship)。自從美國國家醫學圖書館(National Library of Medicine)於 1998 年啟動了 The Visible Human Project [6], 將 CT 與 MRI 的人體切面解剖圖(cross sections)整合, 提供各界一個獨特且重要的人體解剖資料庫, 建構出一個人體解剖的國際性平台。在此厚實的基礎上發展出電腦醫學影像互動式動畫的 3D models, 其中最著名的是 Visible Human 3D Anatomical Structure Viewer (EPA Lausanne)。

(五) 臨床實境模擬

虛擬實境(virtual reality)技術在解剖學教學的應用上更是具有革命性的發展[5]。以腦部神經解剖學為例, 學生藉由動態的3D立體化醫學影像解剖過程, 不僅能對複雜的神經解剖構造有更3D立體化的瞭解, 同時也能有效地模擬真實的神經外科手術進行中可能面對的困難與挑戰, 進而學習神外手術路徑 (neurosurgical approach) 的方法。

電腦醫學影像技術的進步, 不僅促進了臨床影像診斷的品質, 同時也提供不同於以大體解剖為主的解剖學教學方法, 甚而能在手術前提供外科住院醫師虛擬的3D立體手術模擬環境, 達成手術教學的目的。其他虛擬實境技術在臨床醫學上的應用包括: 醫學教育、手術前計畫與模擬、病人模擬、精神評估、復健、虛擬內視鏡、虛擬CPR等[5]。因此, 電腦動畫 3D醫學虛擬實境在臨床醫學的重要性越來越舉足輕重。

(六) 解剖學教材的可重複性

更重要的是, 數位化的醫學影像品質更清晰, 可能的應用與發展性也更廣泛, 同時可以重複提供的解剖學教學工具也更多元化[3,4]。

四. 以電腦醫學影像做解剖學教學的缺點

(一) 缺乏真實的感官經驗

縱使電腦醫學影像技術的進步快速, 但仍然有其先天的限制。醫學生在閱讀臨床醫學影像時, 看到的僅只是人體平面或切面解剖圖(cross sections), 這樣的圖像與實體的解剖構造相較而言非常的抽象, 學生因此無法從其中獲得真實的感官經驗, 進而影響到解剖學的學習。

(二) 對醫學影像的依賴

當醫學生長期使用電腦醫學影像學習解剖學與臨床診斷, 容易產生對醫學影像過度的依賴, 甚而弱化了使用其他診斷工具的能力, 進而影響臨床診療的能力。

討論

一. 主張以電腦醫學影像(computers)為解剖學教學的主要論點

美國解剖學家協會(American Association of Anatomists)於 2002 年的報告顯示: 在美國 141 所學院校裡, 有 14% 的學校沒有大體解剖實驗, 僅以電腦醫學影像來進行教學活動。

而英國的半島醫學院(Peninsula Medical School)創風氣之先, 將大體解剖實驗完全排除於解剖課程教學之外[3], 取而代之的是問題導向學習(PBL)的課程 The four-part approach: 包括有表面及活體解剖學(surface and living anatomy), 醫學影像, 虛擬實境影像(virtual-reality imaging), 及臨床技能模擬器。

作者特別強調: 臨床行醫者常常是透過醫學影像來接觸與了解病人問題, 而透過在臨床技能中心的學習, 由臨床醫師引領醫學生, 統合各種的學習工具, 包括標準病人、醫學影像、模型、與模擬器, 更能在臨床情境下有效學習大體解剖學。捨棄大體解剖實驗的理由是:

1. 從大體解剖實驗獲得的解剖知識無法與臨床醫學影像(以 cross-sectional views 為主) 做有效統合。
2. 從大體解剖實驗獲得的觸感回饋與外科訓練的需要幾乎完全不同。
3. 觀摩大體學習(prosections)可能與體解剖實驗一樣有相等的學習效果。

4. 以脈絡學習的角度而言，在臨床學習之前就早已讀過的大體解剖實驗，很難與臨床學習做有效統合。
5. 大體解剖後壓力症候群，健康風險。
6. 大體解剖實驗的價格昂貴。

二. 主張以大體解剖(cadavers)為解剖學教學的主要論點

大體解剖絕對是解剖學教學的必選課。Granger 在 2004 年強烈的表示：儘管有需多新興的醫學領域 (例如：分子生物學與遺傳基因學)需要被教導，因而壓縮了大體解剖實驗的教學時數，但是，大體解剖實驗依然不能完全被 3D 的虛擬實境 (virtual reality)取代[11]。堅持保留大體解剖實驗的理由是：

1. 對人體構造多面向的理解。
2. 以觸覺來認識人體。
3. 人體解剖構造的多變性。
4. 醫學的基本語言。
5. 有用的技術。
6. 在同儕中學習團隊合作。
7. 簡介醫病關係。
8. 簡介人性化照護的概念與對生死學的理解。

三. 作者的立場(一)：整合式的教學方法(integrated teaching methods)：在電腦醫學影像(computers)與大體解剖(cadavers)的解剖學教學之間，尋求整合。

電腦醫學影像教學與大體解剖實驗是兩種截然不同的解剖學教學方法，兩者的關係表面上似乎是競爭的關係：教學時數的競爭，同時也是教學資源的競爭。

近二十餘年來，有越來越多的研究報告指出：電腦醫學影像輔助教學能夠促進學生解剖學的學習。然而，兩者也可以是整合的關係，有許多的研究指出：透過整合式的教學方法能夠產生增強的效應(synergistic effects)，更有效地促進學生解剖學的學習[3,4,7-9]。

根據愛荷華大學(The University of Iowa)的報告指出，結合解剖實驗與臨床醫學影像(包括 X rays, ultrasound, CT, MRI)的教學法，能夠讓學生解剖學

測驗的正確答題率從 17% 提升到 88%，甚至十多個月後重新測驗的正確答題率也能達到 74% [8]。

而北德州大學(The University of North Texas Health Science Center)的研究也指出：在大體解剖實驗操作時，同步傳送解剖實驗相關的教科書、圖譜內容與臨床醫學影像(包括 X rays, CT, histology)到各個解剖實驗工作站。研究發現：如此整合的教學法能有效增進學生操作解剖實驗的獨立性與專業度，操作解剖實驗的實驗效率，提升解剖學教師實驗教學的品質[9]。

約翰霍普金斯大學附設醫院(Johns Hopkins University Hospital)的報告也指出：合併使用電腦醫學影像(包括 the utility of the Radiological Society of North America-developed Medical Imaging Resource Center, MIRC) 能夠提供醫學生更多元的學習教材，促進學生解剖學的學習[7]。在完成問卷的 85 位醫學生中，87%的學生認為，合併使用電腦醫學影像與傳統解剖教學的教學方法，對於解剖學的學習有幫助。

Biasutto 在 2006 年的報告中顯示[4]：在同時使用大體解剖實驗與電腦醫學影像及軟體作為教材的這組學生，共 145 名，在期末考的分數表現上，明顯比其他兩組學生更好(7.55 vs. 6.17 vs. 6.02)。其他兩組學生各自使用的教材分別是：傳統大體解剖實驗教學或是電腦醫學影像教學。而在期末考的及格率上，同時使用大體解剖實驗與電腦醫學影像及軟體作為教材的這組學生，也有較好的表現(99.23% vs. 60.41% vs. 82.3%)。因此證明：整合式的教學法提供了醫學生更好的教材選擇。同時，他也強調：儘管學生有許多的電腦醫學影像與軟體可供學習，大體解剖實驗依然無法完全被取代。

四. 作者的立場(二)：更好的臨床解剖課(clinical anatomy)

解剖學教學的變革，除了需要在電腦醫學影像與大體解剖實驗這兩種截然不同的解剖學教學方法，做出探討與釐清之外，更重要的是：如何建構一系列更好的臨床解剖課。

(一) 臨床解剖學的重要性！

何謂臨床解剖學(clinical anatomy)？也就是以臨床為導向的解剖課程(clinically oriented approach

to anatomy education)。直接的說也就是：臨床醫學生及臨床醫師需要的解剖學。臨床醫療需要的解剖學知識主要有兩大類：外科解剖學(surgical anatomy)與放射影像解剖學(radiological anatomy) [3]。臨床解剖學更是臨床醫師面對病人的問題、臨床實戰時，推理的基礎。

(二) 臨床解剖教育需要課程改革

以「臨床外科與解剖學能力」的觀點來觀察，很多的外科醫師與基礎解剖學老師認為，醫學生的能力十分缺乏。在歐洲，超過 90%的解剖學教師認為教學方法應該革新[1]。而由 Drake 在 2007 年發表的解剖學教學全新的教學模式可以得知[12]：臨床解剖課可以更好，可行的方式是：以臨床導向、case study 的解剖學教學為主幹，結合大體解剖實驗與電腦醫學影像為教學主體內容。因此，當務之急應是以臨床解剖學的角度，來省思解剖學的教學方法可能的改變。其中包括不同的面向有：(1)解剖學課程時數的縮減，(2)臨床解剖師資重組，(3)多元化的教學工具，(4)臨床案例與解剖學知識的融合教學，(5)PBL 教學。

(三) 解剖學課程師資組成的改變

臨床解剖教育需要師資重組。師資由基礎解剖老師(anatomists)、放射科醫師(radiologist)、與外科醫師(surgeon)共同授課、共同研發課程內容。其中，放射科醫師、外科醫師尤其需要負起更多教學的責任，以「臨床醫學需要之解剖學知識」的全新角度，參與解剖學教學方法的改變與創新。

(四) 解剖學課程的改變：三階段的解剖學教學

從脈絡學習的角度來觀察[9]：大體解剖學實驗的教學通常在醫學生時代，醫學生在面對浩瀚的解剖學知識時，往往只能囫圇吞棗，死背硬背。書到用時方恨少！在醫院見實習的時候，醫學生才驚覺自己臨床解剖知識的缺乏。而在大二時學的解剖學卻很難找回、早已忘掉，不知道如何在大七時活用臨床相關的解剖學知識。所以，行醫時，重新閱讀大體解剖學，至為重要。然而當見實習醫師在醫院裡接觸病人、學習臨床醫學時，普遍並沒有一系列由臨床醫師主導的臨床解剖課，供其做系統性、更有效率的學習。因此，在解剖學教學時程的考量上，如何搭配醫學生時代的大體解剖學實驗教學，在「解剖學知識連貫性」的前提下，將不同困難程

度與不同臨床深度的解剖學教學，分布在醫學生的各個學習階段，至為重要。

梁凱坤等人在2006年針對台灣大學醫學院六年級的醫學生進行調查指出[13]，兩階段的解剖學課程(two-stage anatomy curriculum)能夠增進學生對解剖學知識的理解與記憶。其中第一階段的課程在醫學生第三年，共有112小時，包括48小時解剖講授教學、48小時大體解剖實驗課、及16小時PBL教學。第二階段的課程在醫學生第六年，共有192小時，包括六週的大體解剖實驗與講授教學。兩階段的解剖學課程強調：持續將解剖學課程納入在在醫學生臨床見習的課程裡，能夠幫助學生未來在臨床醫學的學習。

Drake在 2007年發表了解剖學教學創新的教學模式[12]：臨床導向式的解剖學教學。以個案討論(case-directed anatomy program)的教材設計整合了大體解剖實驗與電腦醫學影像。其中的個案教材是經過與外科同事的諮詢、研議之後所發展出來。每星期一次兩小時的課，一學年共三十週。整體在醫學院的三年解剖學課程是Longitudinal programs。在醫學院前三年都不時回顧解剖學。第一年使用的教具是：解剖好的大體(prosected cadavers)與電腦醫學影像。第二年：學生以器官的架構複習解剖學、大體解剖實驗。第三年：臨床見習時，主要課程是外科解剖學(surgical anatomy)。這個全新的學習模式包括以下三大部分：

1. 學生在課堂前需預習臨床案例(clinical case)，包括有臨床問題與學習目標。
2. 學生自修教科書及參考其他教學資源已獲得基本的解剖學知識。
3. 每週的解剖學討論課，課後跑台，依序觀察解剖好的大體(prosected cadavers)與電腦醫學影像。

因此，綜上所論，筆者認為，解剖學教學改革後可行的課程內容如下：

1. 第一階段：醫學生第三年，共有 180 小時。包括：一學年共三十週，每週 1 小時解剖講授教學、PBL 教學每週 1 小時的課、每週 4 小時大體解剖實驗課。
2. 第二階段：醫學生第五~六年，共有 180 小時。包括：一學年共三十週，每週一小時臨床解剖

講授教學、每週兩小時臨床 PBL 整合教學，學生以器官的架構複習解剖學，以臨床個案討論的教材設計，整合解剖學知識與電腦醫學影像。

3. 第三階段：畢業後一般訓練醫師第一年(PGY1)，共有 60 小時。臨床 PBL 整合教學每週兩小時的課，以臨床個案討論的教材設計，主要課程是外科解剖學(Surgical anatomy) 與放射影像解剖學(Radiological anatomy)。

(五) 更好的臨床解剖課教學設備

工欲善其事，必先利其器，更好的臨床解剖課也需要更多創新的教學設備。例如：數位 3D 解剖學教學設備的引進，以六維影像系統(dextroscope)為例[10]。上 dextroscope 解剖課時，學生需戴上 3D 立體眼鏡，在互動的虛擬環境中，學生能夠體驗動態式的 3D 立體化醫學影像(包括 CT 與 MRI)解剖過程，從不一樣的視覺角度觀察、研究身體內部構造，以深入地瞭解解剖構造之間更細緻與更精準的 3D 立體空間關係(Spatial relationship)。而英國的 Bristol 大學更是系統性的改善解剖實驗室的相關設備[14]。包括：解剖台的顯示器與攝影設備。更能夠讓相關醫學影像與解剖實驗做有效統合。

(六) 更好的臨床解剖課教學內容

除了更好的教學設備之外，設計出更精緻與臨床實際情境相關的解剖學教學內容，更是刻不容緩。以鄭泳松等人在 2011 年的報告為例[10]，整合神經解剖圖素描及閱讀、臨床影像內容(頭部電腦斷層題目的前測與後測)與 3D 立體醫學影像的統合式教學法，可以有效降低醫學生的神經學焦慮，更能促進對神經解剖學的學習。

再以 Chariker 等人在 2011 年的研究為例[15]，合併使用 3D 人腦模型與切面解剖(sectional anatomy)，再輔以反覆的測驗與回饋，能夠促進對神經解剖學的學習與長期記憶。

因此，解剖學的教學內容，絕對不能一成不變。需要更多的人力投入與臨床實際情境相關的解剖學教學內容的研發，來幫助醫學生學習解剖學。

五. 作者的立場(三)：以虛擬實境(virtual reality)有效整合基礎與臨床解剖學教學

(一) 學生學習解剖學時面臨的困難

解剖學的學習之所以對醫學生而言，是既困難又充滿挑戰的[15]，原因如下：(1)大量的知識需要在短時間內被理解。(2)解剖構造的形狀不規則與不易辨識。(3)解剖構造在色澤與質地的差異度低。(4)解剖構造相對的3D立體關係複雜。(5)臨床醫學影像切面解剖(sectional anatomy)的學習十分困難。

更好的解剖學教學無非是要幫助醫學生學習，解決醫學生學習解剖學時面臨的困難。然而，如何克服學生學習解剖學時面臨的困難？最主要的方法有二：(1)基礎與臨床解剖學的有效整合，(2)促進學生對於各種解剖學知識的認知重整(cognitive reconstruction)。

(二) 以外科解剖學(surgical anatomy)有效整合基礎與臨床解剖學教學

由於解剖學的學習對醫學生而言十分的困難，因此，當醫學生在醫院裡學習臨床醫學時，更是需要一系列的臨床解剖課，供其做系統性、更有效率的學習。而以外科解剖學(surgical anatomy)作為主要教學內容的理由：是因為外科解剖學最能有效整合基礎與臨床解剖教學，包括手術路徑(surgical approaches)，放射解剖學，與基礎解剖學(basic anatomy)。

在由外科醫師主導的外科解剖學課程中，醫學生對解剖學的學習更能夠得到適當的指導。在手術路徑(surgical approaches)的學習中，醫學生就必須先懂得病灶附近相關的影像解剖，進一步與基礎解剖學中的構造與生理功能的知識做結合，然後在外科醫師的提綱挈領下，手術相關的風險、如何避免併發症、以及術後的照顧等的教學，都能夠幫助學生將基礎解剖學的知識與臨床醫學做結合，對於解剖學的學習最為重要。例如：小腸切除切過多可能會造成 short bowel syndrome、corpus callosum 的 splenium 被切開時，可能會造成 dissociation syndrome。

(三) 以虛擬實境(virtual reality)有效整合基礎與臨床解剖學教學

虛擬實境技術在臨床醫學上的應用包括：醫學教育、手術前計畫與模擬、病人模擬、精神評估、

復健、虛擬內視鏡、虛擬CPR等[5]。其中尤其是醫學教育與外科手術的實境模擬更顯重要。

以神經外科腦部手術為例，越來越多的腦瘤與顱內血管病變運用其他的方式來做治療，例如：放射手術(radiosurgery)或血管內手術(endovascular surgery)。開顱手術的減少勢必會讓年輕的神經外科醫師更難發展相關的外科技術。虛擬實境技術有效地模擬真實的神經外科手術進行中，可能面對的困難與挑戰，進而提供學習神外手術路徑(neurosurgical approach)的方法。

電腦醫學影像的進步，不僅讓數位化的影像品質更清晰，同時也將解剖學教學帶入3D解剖學教學的時代。透過3D立體化的虛擬實境(virtual reality)技術，在互動的虛擬環境中，學生能夠體驗動態式的3D立體化醫學影像解剖過程，從不一樣的視覺角度觀察、研究身體內部構造，以深入地瞭解解剖構造之間更細緻與更精準的3D立體空間關係(spatial relationship)。因此，在虛擬實境(virtual reality)的學習環境中，由於學習的教材是醫學影像，學習的內容是基礎解剖學的知識，醫學生因而最能夠有效統整基礎解剖學與臨床放射解剖學的知識[10]。

綜上所論，若能採用外科解剖學作為教學內容、以個案討論及PBL作為主要的教學方法，進一步使用虛擬實境的影像技術，相信一定能有效整合基礎與臨床解剖學教學，讓醫學生獲得最好的學習。

結論

電腦醫學影像教學與大體解剖實驗是兩種截然不同的解剖學教學方法，兩者的關係表面上似乎是競爭的關係，然而，兩者也可以是整合的關係，電腦醫學影像輔助教學能夠促進學生解剖學的學習，透過整合式的教學方法能夠產生增強的效應，更有效地促進學生解剖學的學習。

解剖學教學的變革，除了需要在電腦醫學影像與大體解剖實驗這不同的解剖學教學方法，做出探討與釐清之外，更重要的是：如何建構一系列更好的臨床解剖課。包括：(1)臨床解剖師資重組，(2)解剖學課程的改變，(3)更好的臨床解剖課教學設

備與教學內容。

電腦醫學影像的進步，不僅讓數位化的影像品質更清晰，同時也將解剖學教學帶入3D解剖學教學的時代，在虛擬實境的學習環境中，若能採用外科解剖學作為教學內容、以個案討論及PBL作為主要的教學方法，相信一定能有效整合基礎與臨床解剖學教學，達成最好的教學效果。

聲 明

本研究之利益衝突：無。知情同意：無。受試者權益：無人體或動物實驗。

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The New Approach of Teaching Anatomy: From Cadaver Dissection to Virtual Reality

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Abstract: Human anatomy has been regarded as the keystone of medical knowledge for centuries. Cadaver dissection is the prevailing pedagogy adopted in most medical schools for anatomy learning. However, with the rise of new computer technology, radiology and digital medical images provide an alternative perspective to approach human anatomy. Hence, “Can traditional cadaver dissection be replaced by new computer-based anatomy teaching?” must be inquired. Here, we also try to explore the role of virtual reality in anatomy teaching. This study reviews and analyzes the current literatures in terms of anatomy education worldwide. We aim to look into the challenges most medical students confront in learning anatomy, and further provide a valid teaching strategy to diminish the current gap in between basic and clinical anatomy.

Key Words: anatomy education, cadaver, computer, clinical anatomy, virtual reality

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請將以下英文翻譯

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An SSVEP-Based BCI Using High Duty-Cycle Visual Flicker

Po-Lei Lee*, Member, IEEE, Chia-Lung Yeh, John Yung-Sung Cheng, Chia-Yen Yang, and Gong-Yau Lan*

Abstract—Steady-state visual-evoked potential (SSVEP)-based brain-computer interfaces (BCIs) have generated significant interest due to their high information transfer rate (ITR). Due to the amplitude-frequency characteristic of the SSVEP, the flickering frequency of an SSVEP-based BCI is typically lower than 20 Hz to achieve a high SNR. However, a visual flicker with a flashing frequency below the critical flicker-fusion frequency often makes subjects feel flicker jerky and causes visual discomfort. This study presents a novel technique using high duty-cycle visual flicker to decrease user's visual discomfort. The proposed design uses LEDs flashing at 13.16 Hz, driven by flickering sequences consisting of repetitive stimulus cycles with a duration T ($T = 76$ ms). Each stimulus cycle included an ON state with a duration T_{ON} and an OFF state with a duration T_{OFF} ($T = T_{ON} + T_{OFF}$), and the duty cycle, defined as T_{ON}/T , varied from 10.5% to 89.5%. This study also includes a questionnaire survey and analyzes the SSVEPs induced by different duty-cycle flickers. An 89.5% duty-cycle flicker, reported as a comfortable flicker, was adopted in a phase-tagged SSVEP system. Six subjects were asked to sequentially input a sequence of cursor commands with the 25.08-bits/min ITR.

Index Terms—Brain-computer interface (BCI), electroencephalographic (EEG), steady-state visual-evoked potentials (SSVEPs).

I. INTRODUCTION

BRAIN-COMPUTER interfaces (BCIs) enable users to communicate with external environments independent of their peripheral neuromuscular functions. Several brain-imaging modalities, such as electroencephalography (EEG), magnetoencephalography (MEG), functional magnetic resonance imaging

(fMRI), positron-emission tomography (PET), and near-IR spectroscopy (NIRS) have been adopted BCIs by measuring neurophysiological signals or hemodynamic changes [1], [2]. The EEG measures the electric field generated from brain cortex and is chosen as the most common tool, due to its advantages of low cost, portability, and high temporal resolution. Many patients with motor disabilities, such as amyotrophic lateral sclerosis (ALS), severe cerebral palsy, head trauma, multiple sclerosis, or muscular dystrophies, are currently using EEG-based BCIs as a communication channel [3].

Steady-state visual-evoked potential (SSVEP)-based BCIs have seen wide applications in recent years due to their unique features of fast-response, high information transfer rate (ITR) (>25 bits/min [4]), relatively few EEG channels, and minimal user training [5]–[9]. SSVEP-based BCIs are often designed by designating different flickers for distinct frequencies (frequency-coded SSVEP-based BCI) [7], [10], [11] or distinct phases (phase-tagged SSVEP-based BCI) [12].

This study develops an SSVEP-based BCI using a high duty-cycle flicker with alpha-band flashing frequency. Many studies have investigated alpha-band SSVEPs as a functional index. Keil *et al.* [13] used a 10-Hz SSVEP to examine emotional processing resources in the human brain when viewing pleasant and unpleasant pictures. Silberstein *et al.* [14] studied the relationship between temporal changes in a 13-Hz SSVEP topography and Wisconsin card sort (WCS) test. They found that the prefrontal, central, and right parieto-temporal regions showed a pronounced attenuation in the SSVEP amplitude and an increase in the phase lag after a change in card sort criteria. Researchers also utilized the 13-Hz SSVEP to examine EEG topography in low and high demand of an object working memory task, showing that the SSVEP amplitude exhibits a load-dependent increase at frontal and occipito-parietal sites [15]. Ding *et al.* [16] studied the effects of attentional modulation by comparing the SSVEP power in gazing at attended visual stimuli to gazing at unattended stimuli, and discovered an increasing SSVEP magnitude in the occipital-frontal network. Thompson *et al.* [17] used a 13-Hz SSVEP indicator to target nicotine-induced cortical activations.

Due to the amplitude-frequency characteristic of the SSVEP, the human SSVEP has larger amplitudes from alpha to low beta ranges and reaches its maximum amplitude at approximately 13 Hz [7], [18]. Flickers with frequencies higher than 31 Hz typically produce poor SSVEP response and a weaker SNR. Advanced signal processing (e.g., the Hilbert–Huang transform) [19] or average over multiple epochs (≥ 60 epochs) [12] is usually required to enhance the SSVEP for systems with high flickering frequencies (≥ 31 Hz). Therefore, most SSVEP-based BCIs use flickering frequencies lower than 20 Hz for

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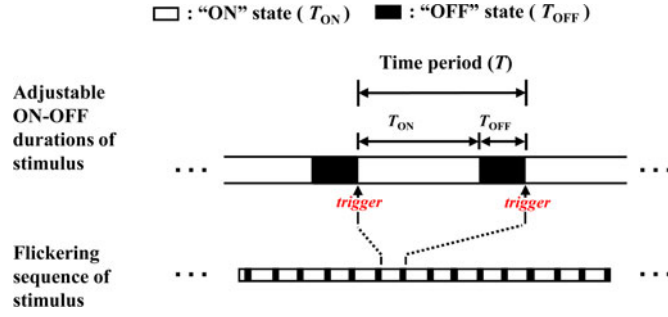


Fig. 1. Flickering sequence with adjusted duty cycle.

visual flickers to retain a high signal level [7]–[9], [20]. However, visual stimuli lower than the critical flicker-fusion frequency (~ 26 Hz in healthy subjects) [21]–[24] will psychophysically make subjects to feel flicker jerky and cause visual discomfort. Accordingly, an SSVEP technique that achieves the high SSVEP amplitude and is comfortable to view is needed.

II. MATERIALS AND METHODS

A. Visual Stimulation

LEDs (part: LYBSB93W1303R012BP, LedTech Electronics Co., Taiwan; rise time $< 50 \mu\text{s}$; wavelength ranging from 400 to 700 nm), covered with thin white paper diffusers, were used as visual stimuli. The LEDs were placed 60 cm in front of subjects to induce SSVEPs. Each LED was driven by a flickering sequence consisting of repetitive stimulus cycles at a 13.16-Hz flashing frequency. Each stimulus cycle had a duration of T ($T = 76$ ms), representing one ON and one OFF cycle with durations T_{ON} and T_{OFF} ($T = T_{\text{ON}} + T_{\text{OFF}}$). The duty cycle R_{duty} was defined as T_{ON} divided by the duration of the stimulus cycle T , i.e., $R_{\text{duty}} = T_{\text{ON}}/T$ (see Fig. 1). The LED luminance was calibrated using a luminance meter (LS-110, Konica Minolta Photo Imaging Inc., USA) and set at 150 cd/m^2 .

The experiments in this study include a questionnaire survey, a flicker investigation study, and a BCI application study. The questionnaire survey was designed to understand user's psychological responses to different duty-cycle flickers; the flicker investigation study investigated the ability of different duty-cycle flickers to induce the SSVEP; the BCI application study tested the feasibility of implementing an SSVEP-based BCI using a high duty-cycle flicker. The questionnaire survey and the flicker investigation study included thirteen 13.16-Hz flickers with different duty cycles, which were 10.5%, 18.4%, 26.3%, 34.2%, 42.1%, 50%, 57.9%, 65.8%, 73.7%, 81.6%, and 89.5% ($T_{\text{ON}} = (2 + i \times 6) \text{ ms}$, $T_{\text{OFF}} = 76 \text{ ms} - T_{\text{ON}}$; $i = 1, 2, \dots, 11$).

In the BCI application study, six visual flickers, named LED₁ to LED₆, were driven by the 13.16-Hz flickering frequency with 89.5% duty cycle ($T_{\text{ON}} = 68 \text{ ms}$ and $T_{\text{OFF}} = 8 \text{ ms}$). The i th visual flicker (LED _{i}) was tagged with the phase delay θ_i , where $\theta_i = (i-1) \times 60^\circ$, $i = 1, \dots, 6$, so that the phase angles were equally distributed over a full 360° phase cycle. The phase delay in an LED was achieved by setting a time delay in its

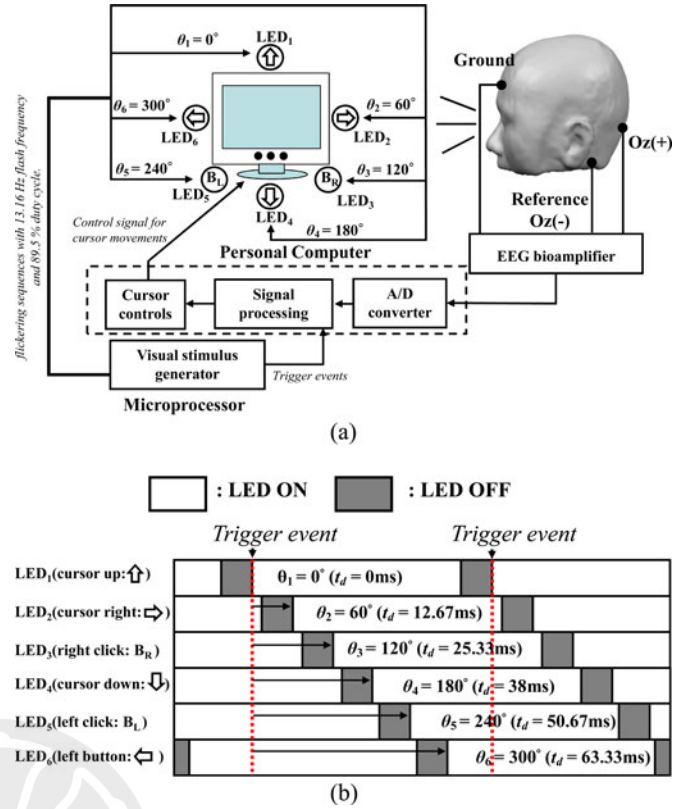


Fig. 2. (a) Schematic diagram of the proposed SSVEP-based BCI system. (b) Six phase-tagged flickering sequences with the 13.16-Hz flashing frequency, 89.5% duty cycle, and 60° phase delay.

flickering sequence:

$$t_i = \frac{\theta_i}{360^\circ} \times T \quad (1)$$

where θ_i is the phase delay assigned to the i th LED, t_i is the requisite time delay for achieving θ_i , $T = 1/f$ is the duration of time block ($T = 76$ ms), and f is the flashing frequency set at 13.16 Hz in this paper. The six LEDs were placed around a computer monitor in clockwise order [see Fig. 2(a)]. LED₁ to LED₆ were used to control six cursor functions ($\uparrow$: “cursor up,” $\rightarrow$: “cursor right,” B_R : “right click,” $\downarrow$: “cursor down,” B_L : “left click,” and $\leftarrow$: “cursor left”).

Fig. 2(b) shows the six phase-tagged flickering sequences with 89.5% duty cycle, where the phase delay was set at 60° ($\pm 30^\circ$ phase margin). Since the flickering sequences were generated at 13.16 Hz (76-ms duration cycle), the phase delays for LED₁ to LED₆ were 0° , 60° , 120° , 180° , 240° and 300° , respectively, corresponding to time delays of 0, 12.67, 25.33, 38, 50.67, and 63.33 ms using (1).

The flickering sequences for driving all LEDs were generated by a microprocessor (dsPIC30F4011, Microchip Technology Inc., USA), programmed with MPLAB IDE software. The flash onsets (from OFF states to ON states) in the flickering sequences served as trigger events for the subsequent averaging process.

B. Questionnaire Survey

Thirty volunteers (twenty males and ten females) aged 23 to 33 years, with normal or corrected to normal vision, were recruited to participate in the questionnaire survey. Each volunteer had a corrected Snellen visual acuity of 6/6 or better, with no history of visual disease.

Thirty volunteers gazed at thirteen 13.16-Hz flickers one-by-one in a random order, with the 30-s duration for each flicker. After gazing at each flicker, volunteers were asked to take a 1-min rest and report their psychophysical feeling perception of visual comfort on a discrete five-point satisfaction scale. The scales were graded as follows: 1 = unacceptable; 2 = uncomfortable; 3 = acceptable; 4 = comfortable; and 5 = delightful. Psychological feelings about visual comfort with the presented flicker were recorded for each volunteer. To avoid influencing their subjective perception, no hint was provided to the volunteers that they could be selected to continue participating in the extended studies. Six of the 30 volunteers (five males and one female), who reported the top six highest mean satisfaction scores in the questionnaire survey (i.e., were less sensitive to flicker jerky), were chosen as subjects for subsequent EEG analysis, including a flicker investigation study and a BCI application study.

C. EEG Recordings and Tasks

Each of the six subjects was requested to sit in a comfortable armchair in a dimly lit room. One EEG bipolar channel was used: an electrode [Oz(+)] placed at Oz position with respect to an reference electrode [Oz(-)] placed at the right mastoid. The ground electrode was placed in the frontal position Fpz. These EEG electrode placements were based on the international EEG 10–20 systems [25]. Oz EEG signals were amplified, prefiltered within 0.1–100 Hz (MacLab, BioAmp, ADInstruments, Castle Hill, Australia) and, then, digitized at 1-kHz (NI-USB 6259E, National Instruments Inc., USA) for further processing. All subjects gave informed consent and the study procedures were approved by the Ethics Committee of Institutional Review Board, Taipei Veterans General Hospital, Taiwan.

The flicker investigation study presented thirteen 13.16 Hz flickers with duty cycles of 10.5%, 18.4%, 26.3%, 34.2%, 42.1%, 50.0%, 57.9%, 65.8%, 73.7%, 81.6%, and 89.5% to the six subjects, one after another, in a random order. Each flicker was presented for 30 s, and the EEG signal at the Oz position was recorded as an EEG recording.

In the BCI application study, subjects were asked to gaze at LED₁ ($\theta_1 = 0^\circ$) for 1-min recording to generate a reference SSVEP, called SSVEP_{ref}, for subsequent gazed-target identification. In the BCI application study, all subjects attempted to control a cursor by producing a sequence of six commands “ $\uparrow \Rightarrow B_L \Downarrow B_R \Leftarrow$ ” three times. The gazing target was detected every 1 s, and valid cursor commands required subjects to keep gazing at the same LED for three successive times. Once a valid input was achieved, a voice feedback informed the subject whose command was just executed. Fig. 2(a) illustrates the architecture of the SSVEP-based BCI system in, including a visual stimulus generator, an EEG bioamplifier, and a PC for signal process-

ing and cursor control. The aforementioned procedures were real-time processed on a PC using LabView software (National Instrument Inc., USA).

D. Signal Processing in the Flicker Investigation Study

The flicker investigation study and the BCI application study use different signal-processing procedures, since they were designed for distinct purposes. The flicker investigation study used the Fourier technique to understand the frequency compositions of the SSVEPs induced by different duty-cycle flickers, while the BCI application study only measured the phase lags of SSVEPs to actuate a phase-tagged BCI.

1) *Flicker Investigation Study*: Each EEG recording (30 s) was first segmented into 1-s EEG segments (30 segments for each EEG recording) based on trigger events and, then, averaged as an SSVEP. The Fourier spectrum of each SSVEP was analyzed using the fast Fourier transform (FFT). The amplitudes of fundamental (13.16 Hz) and first harmonic (26.32 Hz) components for each Fourier spectrum were measured as indices to compare the differences among SSVEPs induced by different duty-cycle flickers. To alleviate interindividual variations in SSVEPs, this study uses a ratio between the amplitudes of fundamental frequency and first harmonic frequency denoted as R_f .

2) *BCI Application Study*: The signal-processing procedure given in [12] is followed. The EEG signals recorded from the Oz position were first bandpass filtered with 10–15 Hz (sixth-order, IIR Butterworth filter) to obtain SSVEP responses and, then, segmented into 76-ms epochs anchored to the trigger events. Epochs were averaged to obtain SSVEP_{gaze}. Note that LED₁ was used to estimate the subject-specific phase lag in performing the cursor control task. The SSVEP_{ref} induced by LED₁ was generated by averaging the epochs in the 1-min recording before the cursor control task. The latency of the maximum amplitude peak in SSVEP_{ref}, denoted by t_{ref} , was measured for the following signal processing.

The recognition of user's gazed target in phase-tagged SSVEP-based BCI was based on detecting the phase lag between the SSVEP_{gaze} and the SSVEP_{ref}. The procedure for gazed-target identification involved several steps. First, an epoch-average process was applied to average across the latest N ($N = 13$) epochs in the epoch register to obtain an SSVEP_{gaze} every 1 s. Second, since the detection of phase lag can be achieved by measuring the time shift between SSVEP_{gaze} and the SSVEP_{ref}, the latency of maximum amplitude peak in SSVEP_{gaze} is detected and designated as t_{peak} . Third, the time lag t_d between t_{peak} and t_{ref} was calculated, i.e., $t_d = t_{peak} - t_{ref}$. Fourth, since the flickering frequency f ($f = 13.16$ Hz) and duration cycle T ($T = 76$ ms) are known, the phase $\theta_{detected}$ between the SSVEP_{gaze} and the SSVEP_{ref} is

$$\theta_{detected} = \frac{t_d}{T} \times 360^\circ. \quad (2)$$

$\theta_{detected}$ was further readjusted within 0° and 360° to obtain the phase lag θ_d by

$$\theta_d = \theta_{detected} + 360^\circ \times r \quad (3)$$

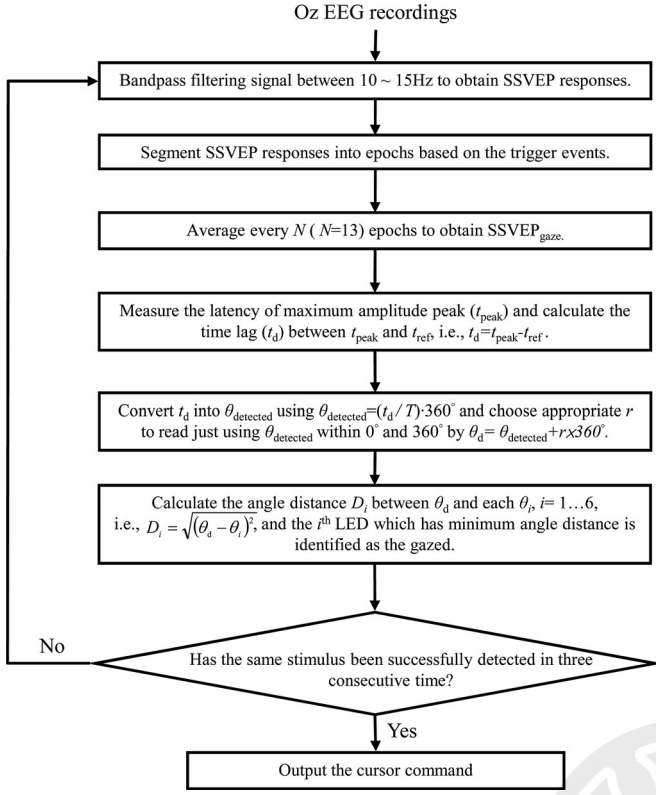


Fig. 3. Overall flow chart for the signal processing of the proposed SSVEP-based BCI system.

where r is an appropriate integer to confine the phase lag θ_d within 0° and 360° . Fifth, the angle distances between θ_d and the expected phase delays ($\theta_i, i = 1, \dots, 6$) were calculated, i.e., $D_i = \sqrt{(\theta_d - \theta_i)^2}$. The i th LED (LED _{i}) with the minimum angle distance D_i was identified as the gazing target [12]. Sixth, once a same gazed target was detected for three successive times, the gazed target was recognized as valid and its corresponding cursor command was activated. Fig. 3 summarizes this process.

This study fulfills the four prerequisite conditions for the ITR calculation, which are 1) K selections are possible, 2) each selection has the same probability, 3) the specific accuracy is the same for each selection, and 4) each undesired selection has the same probability of selection [26]. The accuracies, command transfer intervals (CTIs), and ITRs were computed to evaluate users' performance. The ITR was computed as [4], [5]

$$\frac{\text{Bits}}{\text{command}} = \log_2 K + P \log_2 P + (1 - P) \log_2 \left[\frac{(1 - P)}{(K - 1)} \right] \quad (4)$$

$$\text{ITR} = \frac{\text{Bits}}{\text{command}} \times \frac{60}{\text{CTI}} \quad (5)$$

where K is the total number of visual flickers ($K = 6$) and P is the accuracy.

TABLE I
STATISTICAL RESULTS OF QUESTIONNAIRE SURVEY FROM 30 VOLUNTEERS ABOUT THE RESPONSES OF VISUAL COMFORT TO DIFFERENT DUTY CYCLES

The duty cycles used in 13.16Hz stimulation	Number of participants				
	Satisfaction scale				
	unacceptable	uncomfortable	acceptable	comfortable	delightful
10.5%	26 (86.67%)	4 (13.33%)	0	0	0
18.4%	21 (70%)	9 (30%)	0	0	0
26.3%	14 (46.67%)	14 (46.67%)	2 (6.67%)	0	0
34.2%	7 (23.33%)	17 (56.67%)	6 (20%)	0	0
42.1%	1 (3.33%)	19 (63.33%)	10 (33.33%)	0	0
50.0%	1 (3.33%)	5 (16.67%)	24 (80%)	0	0
57.9%	1 (3.33%)	4 (13.33%)	24 (80%)	1 (3.33%)	0
65.8%	0	4 (13.33%)	20 (66.67%)	6 (20%)	0
73.7%	0	3 (10%)	17 (56.67%)	10 (33.33%)	0
81.6%	0	0	12 (40%)	15 (50%)	3 (10%)
89.5%	0	0	10 (26.67%)	17 (63.33%)	3 (10%)

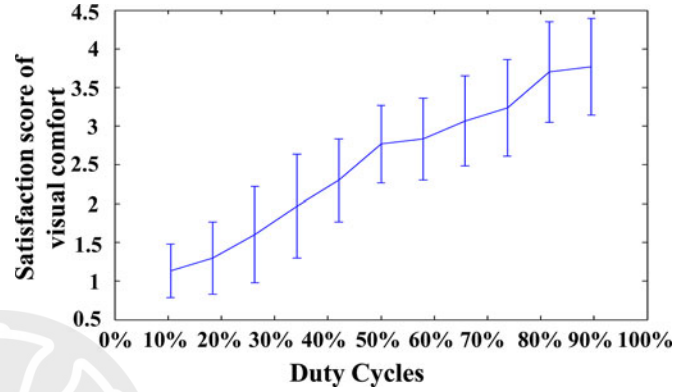


Fig. 4. Satisfaction scores obtained from 30 volunteers in the questionnaire survey.

III. RESULTS

A. Questionnaire Survey

Table I lists the psychological feelings of self-reported visual comfort in response to different duty-cycle flickers. More than 80% of the 30 volunteers reported feeling “acceptable” or better (“comfortable” and “delightful”) when viewing LEDs with duty cycles higher than 50%. For a duty cycle higher than 81.6%, all volunteers reported “acceptable” or better, and more than 60% of the volunteers reported feeling “comfortable” or better. For a flicker with an 89.5% duty cycle, volunteers reported satisfaction scores of 26.67%, 63.33%, and 10% for “acceptable,” “comfortable,” and “delightful,” respectively.

The satisfaction scores (mean $\pm$ std.) obtained from the 30 volunteers were 1.13 ± 0.35 , 1.30 ± 0.47 , 1.60 ± 0.62 , 1.97 ± 0.67 , 2.30 ± 0.54 , 2.77 ± 0.50 , 2.83 ± 0.53 , 3.07 ± 0.58 , 3.23 ± 0.63 , 3.70 ± 0.65 , and 3.77 ± 0.63 for 10.5%, 18.4%, 26.3%, 34.2%, 42.1%, 50.0%, 57.9%, 65.8%, 73.7%, 81.6%, and 89.5% duty cycles, respectively (see Fig. 4). Examining the satisfaction score versus visual comfort, the visual comfort was proportionally improved to the increment of the flicker duty cycle ($r = 0.99$, $p < 0.01$; linear regression). The 89.5% duty-cycle flicker, which achieved the highest satisfaction score, was designated as a comfortable flicker and utilized in the subsequent flicker investigation and BCI application studies. These questionnaire results manifests indicate that the use of high duty-cycle flicker may be a plausible way to improve the visual comfort of flickers.

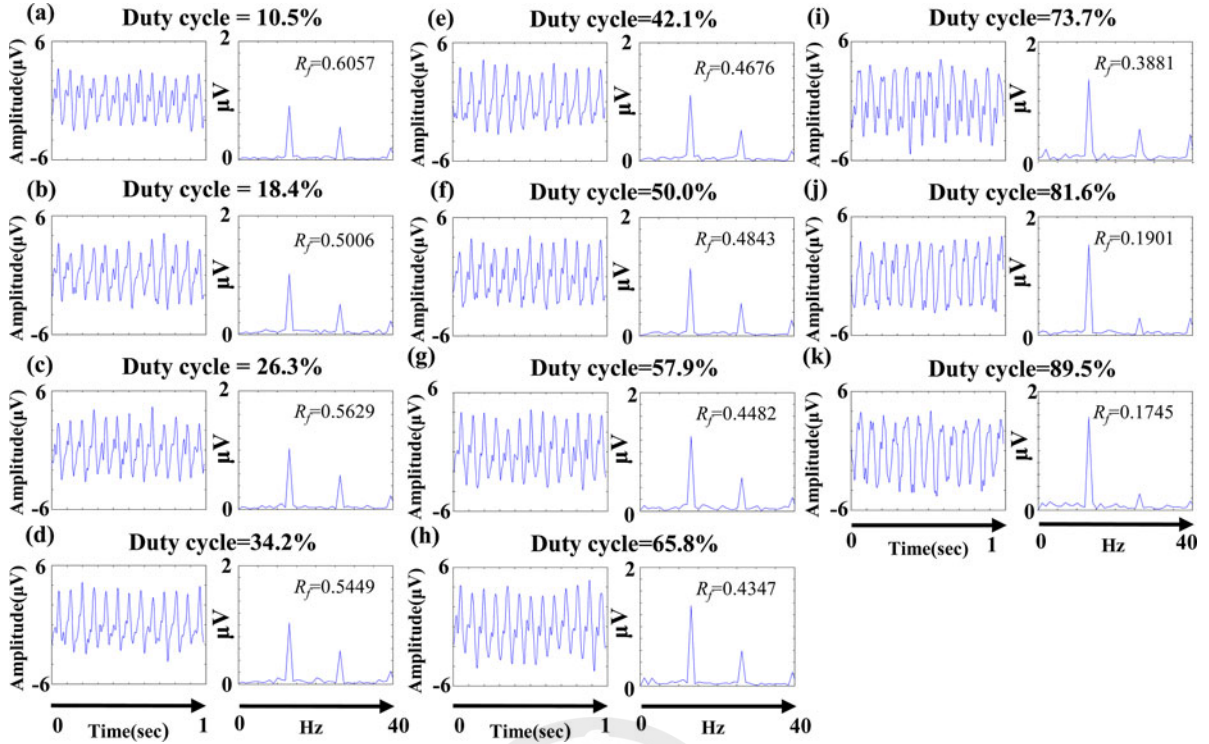


Fig. 5. Temporal waveforms and Fourier spectra of SSVEPs induced by different duty cycles of 13.16-Hz flickers in subject I.

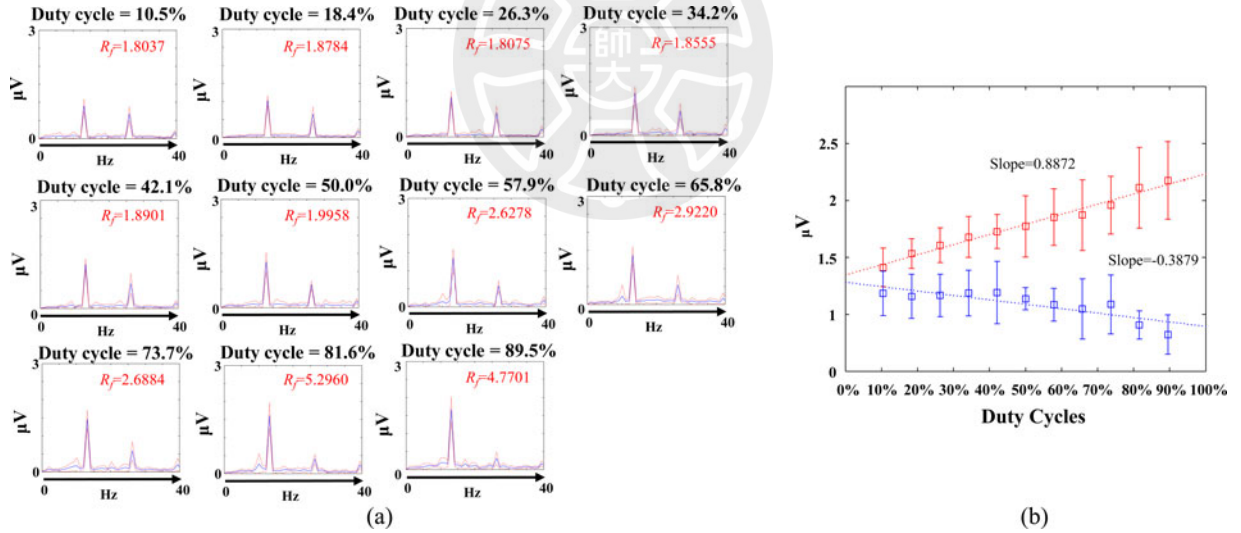


Fig. 6. (a) Spectrum of average SSVEPs for the six subjects. (b) Results of Amp_{base} 's and Amp_{har} 's measured over the six subjects.

B. SSVEPs in the Flicker Investigation Study

Fig. 5 shows the temporal waveforms and the Fourier spectra of SSVEPs obtained from gazing at 13.16-Hz flickers with different duty cycles in subject I. The temporal waveforms of SSVEPs and their Fourier spectra appear in the left and right panels of Fig. 5(a)–(k), respectively. The amplitudes of fundamental components (13.16 Hz), called Amp_{base} , were 0.91, 1.02, 1.02, 1.03, 1.12, 1.14, 1.26, 1.35, 1.36, 1.53, and 1.56 μV , and the amplitudes of first harmonic components (26.32 Hz), called Amp_{har} , were 0.55, 0.51, 0.58, 0.56, 0.52, 0.55, 0.56, 0.58, 0.53, 0.29, and 0.27 μV for flickers with duty cycles of 10.5%,

18.4%, 26.3%, 34.2%, 42.1%, 50.0%, 57.9%, 65.8%, 73.7%, 81.6%, and 89.5%, respectively. The ratios between Amp_{base} 's and Amp_{har} 's, i.e., Amp_{har}/Amp_{base} , denoted as R_f , were 0.61, 0.50, 0.56, 0.54, 0.47, 0.48, 0.45, 0.43, 0.39, 0.19, and 0.17 for 10.5%, 18.4%, 26.3%, 34.2%, 42.1%, 50.0%, 57.9%, 65.8%, 73.7%, 81.6%, and 89.5% duty cycles, respectively, showing an reduction in R_f associated with the increase of flicker duty cycles.

Fig. 6(a) presents the averaged Fourier spectra of SSVEPs (six subjects pooled) under the conditions of gazing different duty-cycle flickers. The solid lines show the averaged spectra and

TABLE II
RESULTS OF AMP_{base} 'S AND AMP_{har} 'S MEASURED OVER THE SIX SUBJECTS

	The duty cycles used in 13.16 Hz stimulation										
	10.50%	18.40%	26.30%	34.20%	42.10%	50.00%	57.90%	65.80%	73.70%	81.60%	89.50%
The amplitudes of fundamental components (AMP_{base})	0.91±0.17	1.03±0.13	1.11±0.15	1.18±0.18	1.23±0.15	1.27±0.27	1.35±0.25	1.37±0.31	1.46±0.25	1.61±0.36	1.67±0.34
The amplitudes of first harmonic components (AMP_{har})	0.68±0.20	0.66±0.19	0.66±0.19	0.69±0.20	0.69±0.27	0.64±0.10	0.58±0.14	0.55±0.26	0.59±0.26	0.41±0.12	0.32±0.17

the dashed lines indicate the averaged spectrum plus/minus the standard deviations. AMP_{base} 's and the AMP_{har} 's values over the six subjects (mena $\pm$ std.) were listed in Table II. Both the fundamental components and the first harmonic components were clearly observed under different duty-cycle conditions, even when an 89.5% duty cycle (68-ms ON state and 8-ms OFF state) was applied. Fig. 6(b) shows the results of AMP_{base} 's and AMP_{har} 's measured over the six subjects. AMP_{base} 's increased significantly with the increase of the duty cycle ($r = 0.8872$, $p < 0.01$; linear regression), while AMP_{har} 's showed a decreasing trend in association with the increase of duty cycle ($r = -0.79$, $p < 0.01$; linear regression). The values of R_f were 0.77 ± 0.34 , 0.65 ± 0.23 , 0.60 ± 0.17 , 0.58 ± 0.15 , 0.55 ± 0.19 , 0.51 ± 0.10 , 0.45 ± 0.15 , 0.41 ± 0.19 , 0.41 ± 0.20 , 0.27 ± 0.11 , and 0.20 ± 0.12 for 10.5%, 18.4%, 26.3%, 34.2%, 42.1%, 50.0%, 57.9%, 65.8%, 73.7%, 81.6%, and 89.5% duty cycles, respectively.

C. Gazed-Target Detections in the BCI Application Study

Fig. 7 shows an example of online signal processing for extracting SSVEPgaze for subject I gazing at LED₂ (phase delay = 60°). Since the identification of gazed target in a phase-tagged system depends on the detection of θ_d between SSVEPgaze and SSVEP_{ref}. The first panel shows the ON-OFF states of the flickering sequence of the LED₂. The raw Oz EEG signal shown in the third panel was bandpass filtered within 10–15 Hz to obtain the SSVEP response (see the fourth panel). The flash onsets of LED₁ flickering sequence, marked by red dashed vertical lines, served as trigger events to segment the SSVEP response into epochs, based on trigger events (every 0.1 s). An epoch-average process was applied to the latest 13 epochs (epoch index shown in the second panel) based on trigger events to obtain SSVEPgaze. The enlarged plot at the bottom shows one SSVEPgaze with t_{peak} detected at 41 ms. The phase delay θ_d is $(41 - 29)/76 \times 360^\circ = 56.84^\circ$, so that the gazed target is LED₂.

Table III shows the results of gazed-target detection for all six subjects. The second column lists the results of all gazed-target detections. Note that a valid command was recognized only when a same gazed target being detected for three successive times. The gazed-target detections used for valid command generations are underlined, while others are left as wrong gazed-target detections (marked in red). All six subjects completed the production of command sequence “B_L $\Downarrow$ B_R $\Leftarrow \Rightarrow$ ” three times. The third column lists the accuracy of gazed-target detection,

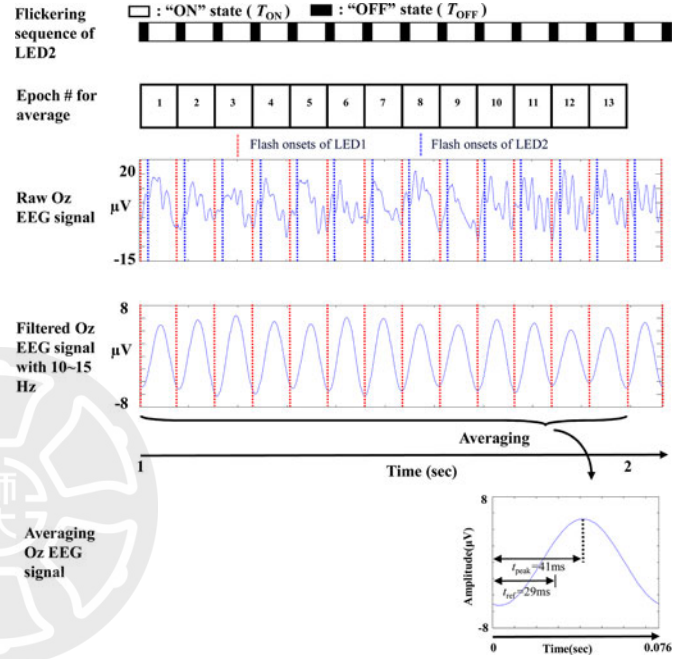


Fig. 7. Signal processing for extraction of the SSVEP when a subject was staring at target LED₂ with designed duty cycle (89.5%) of the fixed stimulation frequency (13.16 Hz).

defined as $N_{correct}/N_{total}$, in which $N_{correct}$ is the number of gazed-target detections used for valid command generations and the N_{total} is the number of total gazed-target detections. The fourth column presents the accuracy of valid command output. The CTI and ITR computed of the six subjects are listed in seventh and eighth columns, respectively. The mean accuracy of gazed-target detection, accuracy of valid command output, CTI, and ITR were 82.08%, 100%, 3.66 s/command, and 25.08 bits/min, respectively.

IV. DISCUSSION

The experiments in this paper used flickers with alpha-band flickering frequency (13.16 Hz) and high duty cycle (89.5%) to induce subject's SSVEPs for BCI control. The questionnaire survey confirms the visual comfort of these high duty-cycle flickers. In addition, due to the high SNR in the SSVEPs induced by alpha-band flickers, these results may provide a feasible way to design visual flickers in SSVEP-based BCIs that retain both high SSVEP amplitude and improved visual comfort.

TABLE III
RESULTS OF PRODUCING STRING " $B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$ " THREE TIMES FROM THE SIX SUBJECTS

Subject index	Results of gazed-target detections (wrong colored by red)		Valid command output	Accuracy of gazed-target detection ($N_{\text{correct}}/N_{\text{total}}$)	Accuracy of valid command output	Total Time (sec)	CTI	ITR
I	1 st trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow B_L \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$	83.08% (54/65)	100%	65	3.61	25.53
	2 nd trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
	3 rd trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
II	1 st trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$	88.52% (54/62)	100%	62	3.44	30.18
	2 nd trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
	3 rd trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow B_L \Rightarrow \Rightarrow \Rightarrow \Uparrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
III	1 st trial	$B_L B_L B_L \Leftarrow \Leftarrow \Leftarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow B_L \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$	78.26% (54/69)	100%	69	3.83	20.75
	2 nd trial	$B_L B_L B_L \Leftarrow \Leftarrow \Leftarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
	3 rd trial	$B_L B_L B_L \Leftarrow \Leftarrow \Leftarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Uparrow \Uparrow \Uparrow B_L \Rightarrow \Rightarrow \Rightarrow \Uparrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
IV	1 st trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow B_L \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$	81.82% (54/66)	100%	66	3.67	24.18
	2 nd trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Downarrow \Downarrow \Downarrow B_L \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
	3 rd trial	$B_L B_L B_L \Leftarrow \Leftarrow \Leftarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow B_L \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
V	1 st trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$	88.52% (54/61)	100%	61	3.39	31.94
	2 nd trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow B_L \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
	3 rd trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Leftarrow \Leftarrow \Leftarrow \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
VI	1 st trial	$B_L B_L B_L \Leftarrow \Leftarrow \Leftarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Downarrow \Downarrow \Downarrow \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$	75% (54/72)	100%	72	4	17.90
	2 nd trial	$B_L B_L B_L \Downarrow \Downarrow \Downarrow \Leftarrow \Leftarrow \Leftarrow B_L B_L B_R B_R B_L \Leftarrow \Leftarrow \Leftarrow B_L \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
	3 rd trial	$B_L B_L B_L \Rightarrow B_L \Leftarrow \Leftarrow \Leftarrow B_R \Uparrow \Uparrow \Uparrow B_R B_R B_R \Downarrow \Downarrow \Downarrow \Rightarrow \Rightarrow \Rightarrow$	$B_L \Downarrow \Uparrow B_R \Leftarrow \Rightarrow$					
Average (mean $\pm$ std.)				82.03 $\pm$ 5.43% (324/395)	100 $\pm$ 0%	65.83 $\pm$ 4.17	3.66 $\pm$ 0.23	25.08 $\pm$ 5.37

The adjustment of duty cycle in a visual flicker actually changes the proportion of ON and OFF states in the duration cycle T ($T = 76$ ms) of the 13.16 Hz flicker. For example, a duty cycle of 89.5% flicker at 13.16-Hz flickering frequency has 68 ms in the ON state ($T_{\text{ON}} = 68$ ms) and 8 ms in the OFF state ($T_{\text{OFF}} = 8$ ms). According to the questionnaire survey, setting higher duty cycle in its flickering sequence can improve visual comfort. No subjects reported visual discomfort when a 13.16-Hz visual flicker with 81.6% duty cycle ($T_{\text{OFF}} \leq 14$ ms) or higher was applied. Since higher duty cycle causes shorter duration in the OFF state, the shortening of interstimulus OFF durations may increase the continuity between adjacent two ON states.

The visual comfort achieved by high duty-cycle flicker may be due to visual persistence, which is the phenomenon of short-period afterimage persistence on the retina [27], [28]. The visual persistence phenomenon has been widely used in monitor systems and cinema industries. It is widely believed that an after-image visual persistence is approximately 1/25 of a second. As a result, a film system with an interpicture interval of less than 1/25 s can reduce flickering image problem. The alleviation of

visual flickering problem can be explained by human's vision capability in resolving two consecutive pulses. Treutwein and Rentschler [29] changed the interpulse interval in a double-pulse discrimination task, in which the stimulus had a leading pulse and a trailing pulse. According to [29], the critical gap duration, which was defined as the duration giving a 55.55% probability of correct resolving the double pulses, was approximately 25 ms for 68 ms leading pulse duration.

This study uses an 89.5% duty-cycle flicker with the 13.16-Hz flickering frequency for BCI control. The stimulus onset asynchrony (SOA) was fixed at 76 ms and the higher duty cycle actually shortened the interstimulus interval (ISI) between two consecutive ON states. Since the ISI at 89.5% duty cycle was only 8 ms, which was shorter than the critical gap duration (~ 25 ms) reported in [29], flicker fusion achieved in an 89.5% duty-cycle flicker could be used for improving visual comfort.

An interesting finding was the effects on Amp_{base} and Amp_{har} , while changing the duty cycles of 13.16-Hz flickers. This flicker investigation study revealed that a higher duty cycle in visual flicker prolonged the ON state and shortened the OFF state, which in turn enhanced Amp_{base} and decreased Amp_{har} .

(see Fig. 6). Previous authors examined the electrophysiological meanings of the fundamental and first harmonic components [30]. They used a 64-channel EEG system to study topographic distribution of the SSVEP induced by a 12.5-Hz flicker and suggested that the fundamental component could reflect broad bottom-up activation of visual cortical areas. In contrast, higher harmonic components (including first harmonic component) are tuned by feedback interactions and are modulated by subject's top-down process, such as voluntary attention.

The positive relation between the duty cycle of visual flicker, and Amp_{base} could be due to the temporal integration of human vision (Bloch's law) [31], [32]. Bloch's law states that the perceived contrast Ψ is linearly determined as a function of stimulus contrast (or intensity I) and stimulus duration t [31] when the stimulus duration is below a critical duration ($t_c = 100$ ms):

$$\Psi = I \cdot t, \quad t \leq t_c. \quad (6)$$

A stimulus duration exceeding the critical duration t_c will not increase its perceived contrast and will present no enhancement on the perceived contrast to a visual stimulus. In this flicker investigation study, the stimulus durations (duration for the ON state), which ranged from 8 to 68 ms, were shorter than 100 ms. Thus, the perceived contrast was increased as the stimulus duration increased. In addition, since the human VEP is a function of light luminance and duration [33], longer stimulus duration or higher luminance will result in a greater VEP response. Therefore, the enhancement of Amp_{base} could be attributed to the longer ON duration in high duty-cycle flicker.

Previous research examines the role of the first harmonic component in arousal stimulation in human EEG studies [30], [34] and in animal studies [35]. The first harmonic response may be altered by the subject's arousal function [35]. Paying attention to repetitive visual stimuli can increase the first harmonic response of the SSVEP [30], [36]. The questionnaire survey in this study reported uncomfortable perception to low duty-cycle flicker. The uncomfortable flicker may draw more of subjects' attention when they were mandated to gaze at the visual flicker. It may excite more first harmonic component under the stimulation of lower duty-cycle flicker. In contrast, a higher duty-cycle flicker achieves better visual comfort, making it possible to obtain a smaller amplitude in the first harmonic component.

Unlike other SSVEP-based BCI systems, $\text{SSVEP}_{\text{gaze}}$ in the proposed phase-tagged system was obtained by an epoch-average process. Oz EEG signals were segmented into 76-ms epochs and, then, averaged according to trigger events. Due to the time-locked and phase-locked characteristics of human VEP [19], [34], SSVEP-unrelated noise (e.g., alpha rhythm, beta rhythm, 60-Hz electricity noise, etc.) was suppressed after the epoch-average process. Therefore, though the alpha-band SSVEP frequency response overlaps with the frequency ranges of occipital alpha and beta rhythms, the fundamental and first harmonic components are still clearly observed in Figs. 5 and 6. The proposed signal-processing procedure can recognize six different phase-tagged 13.16-Hz flickers.

In this study, the volunteers with the top six highest mean satisfaction scores in the questionnaire survey were selected to participate in the following flicker investigation and BCI studies.

The selection of high satisfaction group rises from the rationale that volunteers who were less sensitive to flicker jerky might be more unconscious of perceiving the presented flickers. This may support the idea of nonconscious perception [21], which demonstrated that SSVEP responses can be induced even under nonconscious conditions.

It has been reported that most photosensitive epilepsy patients are sensitive to flashes with flickering frequencies between 9 and 18 Hz [37]. Though the proposed high duty-cycle flickers could achieve better visual comfort than flickers with 50% duty cycle, the influence of high duty-cycle flicker on inducing epileptiform responses in photosensitive epilepsy patients is still unknown. The use of 13-Hz flicker with high duty cycle might be still risky to those photosensitive patients. Further studies are required to evaluate the risks of high duty-cycle flicker stimulation in photosensitive epilepsy patients.

At least two other phase-tagged SSVEP-based BCI systems have been reported. One utilized high-frequency flicker (31.25 Hz; 50% duty cycle) [12], and the other used multiple frequency-phase design (10–15 Hz; 16.67–25% duty cycle) [38]. Both the two systems have demonstrated their high accuracy rates and ITRs. In the high-frequency flicker study [12], the visual comfort was achieved by inducing flicker fusion effect [39], [40], but longer response time (1.92 s versus 0.98 s) and more epoch number (60 epochs versus 13 epochs) were required compared to the present study. In the multiple frequency-phase study, Jia *et al.* [38] achieved high ITR (~ 60 bits/min) in a simulated online test, using low duty-cycle flickers in alpha-range frequencies. However, the main scope of this paper focuses on achieving better visual comfort by means of high duty-cycle flicker. Users' psychological feelings were rated by a questionnaire survey, and the capability of high duty-cycle flicker in inducing the SSVEP was validated by EEG experiments. This study has successfully demonstrated the applicability of the high duty-cycle flicker to implement SSVEP-based BCIs.

V. CONCLUSION

This study presents a phase-tagged SSVEP-based BCI system using high duty-cycle flickers flickering at 13.16 Hz. The feasibility of the proposed system was confirmed by experiments in which participants controlled four cursor movements (up, right, down, left) and two button functions (right and left clicks) on a screen menu. The salient features of the proposed system include: 1) better visual comfort achieved by the high duty-cycle flicker; 2) the availability of high duty-cycle flicker in inducing the SSVEP; and 3) the suppression of SSVEP-unrelated noise by simply applying an epoch-average process in the phase-tagged system. All the six subjects, who participated in the flicker investigation study and the BCI application study were able to successfully input a sequence of cursor commands with acceptable accuracy and high ITR. The proposed system may provide a new visual stimulus design for SSVEP-based BCIs. Results further show that Amp_{base} and Amp_{har} have positive and negative relationships with an increase in the flicker duty cycle, respectively. However, future studies involving more subjects may be required to confirm this phenomenon.

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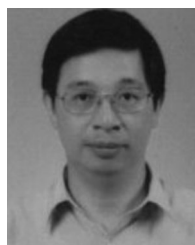
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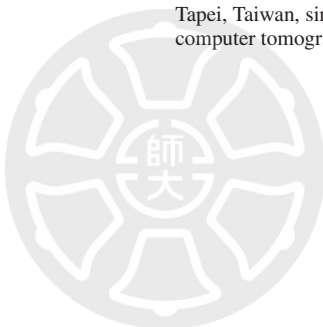
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Oral papers 02

- **The nature of abacus is one kind of working memory training: a functional MRI and behavior study.**

John Yung-Sung Cheng, MD; Chun-Yen Chang, PhD

國際研討會名稱 : STEM 2014, 12-15th, July, the University of British Columbia in Vancouver.

Abstract With aid of educational neuroscience, we can take a different perspective on the traditional Chinese tool for calculation. The aims of our unique longitudinal study are to evaluate the relatively short term effect of six-months abacus-based mental calculation (AMC) training on the functional connectivity network, and to investigate the possibility of AMC training effect transfer to the untrained working memory task. Abacus experts have demonstrated extraordinary potential of mental calculation in the past cross-sectional studies. Non-experts show activity in the prefrontal and perisylvian areas, while experts, with long-term training of at least three to five years, show more activation over premotor and parietal regions. The trained children advanced 9.11 percentile on the WISC-IV exam's working memory subsection (from 81.19 to 90.30, $p = 0.037 < 0.05$). Resting state MRI revealed increased connectivity between the left inferior frontal area and the left inferior parietal lobe. The combined results suggested six months of AMC training can generalize to untrained working memory exams, and a midway paradigm shift can be expected along the fronto-parietal circuitry within the relatively long time required to become an expert. Compared to the common practice of task repetition, AMC is not only an arithmetic operation, but an appropriate and interesting tool to improve working memory capabilities by exercising visuo-motor and visuo-spatial skills.

Keywords: abacus, abacus-based mental calculation, functional connectivity, resting state, working memory, working memory training

Goals and objectives

The goals of our study are as following: (1) to evaluate the relatively short term effect of six-months abacus-based mental calculation (AMC) training on the functional connectivity network, and (2) to prove the possibility of AMC training effect transfer to the untrained working memory task.

Theoretical framework

With a history tracing back various millenniums in different cultures, the abacus is an essential tool to human civilization growth and development. It is also a significant symbol in Chinese culture for trade and calculation. Inscription of Chinese abacus on the Representative List of the Intangible Cultural Heritage of Humanity was announced on December 2013 by UNESCO for its cultural significance and "training in abacus-based mental arithmetic is thought to improve a child's attention span, memory and mental capability." (1) Abacus experts have demonstrated extraordinary potential of mental calculation (2), and even beginner youths are often expected to improve in attention and mental focus abilities. Past imaging studies show a significant difference between experts and non-experts in brain functional areas when performing mathematical tasks (2-5). Non-experts show activity in the prefrontal and perisylvian areas, while experts with long-term training show more activation over premotor and parietal regions. Most abacus-related studies in the past have cross-sectional designs, comparing abacus experts with non-experts. However, in the current Chinese social norm, with the availability of more active or creative extracurricular courses, very few children have the opportunity or willingness to pursue further abacus training after the initial one to two years, far less than the necessary training to become an expert. Therefore, we are curious about the effects of short-term abacus training on functional and behavioral levels. More importantly, how soon can we expect change after initializing training on the functional level and the behavioral level? Children in Chinese society are encouraged to study for at least six months to one year to become acquainted with abacus-based mental calculation (AMC) and express significant behavioral improvement. The Chinese Abacus Association in Taiwan states that in past experience, the greatest level of behavioral improvement is shown after six months to one year. Irwing et al. suggested in 2008 a general intelligence improvement after receiving only 34 weeks of abacus training(6). Hu et al. suggested in 2011 potential enhancement on white matter integrity after abacus training for 3 years (7). Takeuchi et al. showed in 2013 cognitive training can have probable effects on intrinsic brain activity and connectivity (8). In this study, we hypothesize potential midway paradigm drift, significant change in visuo-motor and visuo-spatial regional connectivity, and working memory behavioral improvement

within a six-month abacus training period. After deploying standardized tests, functional MRI (fMRI), and resting state MRI (rsMRI), we evaluate the validity and scale of this change on both the behavioral level and the functional level under a relatively short-term training curriculum.

Methodology

A total of forty-three healthy right-handed children participated in this study. The subjects are split into two groups: abacus training (ABA, $n=21$, 17 females, mean age = 9.61 years) and reading control (CON, $n=22$, 16 females, mean age = 10.57). Two abacus-based mental calculation (AMC) teachers were recruited to provide training for the ABA group over a six-month period. The group received 3.5 hours of training per week (2 hours of teacher-student lessons and 1.5 hours of practice homework) for 25 weeks. The CON group performed general reading exercises for 3.5 hours per week for 25 weeks. The total effective training time was 87.5 hours. The subjects were examined with fMRI, rsMRI functional connectivity (FC), and behavioral exams before and after the six-month training period. Abacus rating exams for the ABA group were provided at the end of the training period by the Chinese Abacus Association. The subjects were asked to perform a simple serial addition task (SSA) during the fMRI scan. The task initialized with the presentation of a plus-sign visual stimulus of 15 seconds, followed by a control or task period of 24 seconds. The control block presented ten eight-digit random numbers presented in series with frequency of 0.5 Hz and subjects were required to gaze at the numbers without calculation. The task session presented ten random one-digit numbers with the same frequency and the subjects were instructed to sum the presented digits. At the end of each task block, the subjects are asked to select by mouse-click the correct sum from a queue of two numbers. During the rsMRI scan, subjects were instructed to keep their eyes closed, remain clear-minded, and think of nothing in particular. The fMRI images were acquired with a 1.5 T MAGNETOM Avanto system (Siemens) using a T2*-weighted gradient-echo echo-planar imaging (EPI) sequence (TR/TE/FA = 3000 ms/50 ms/90°). For each subject, 104 volumes of 20 axial slices per volume were acquired. Resting state acquisitions were performed with the same sequence except TR = 2000 ms and total volume = 180. After each image acquisition, the WISC-IV exam's working memory subtasks (including digit span, letter-number sequencing, and arithmetic subtests) were deployed to examine the subjects' working memory capabilities, and an anxiety score questionnaire was used to evaluate the level of anxiety the subjects felt towards mathematical processing and towards the MRI examination. Statistical analyses of functional images for regions of significant change were accomplished using a multi-step process using SPM5 (9) and REST (10). The EPI data was realigned and spatially normalized into MNI template, then

smoothed with a Gaussian kernel of 6 mm. Functional activations were obtained by modeling the data with GLM and group results were analyzed using one sample t-test. For rsMRI, after preprocessing, FC images underwent seed-based correlation analysis. Left prefrontal seeds were selected from the results of a task-related fMRI pilot study (11) (Table 1) including left fronto-insular cortex and left Broca area (LBA.) The correlated results were transformed to approximate Gaussian distribution using Fisher's z transformation. Between-group and within-group comparisons were assessed by unpaired two-sample and paired two-sample t-tests respectively. For regression analysis, the ROIs were selected from activated prefrontal and parietal clusters determined using the anatomical automatic labeling (AAL) template (12), including left inferior frontal gyrus (LIFG) and left angular gyrus (LAG).

Results

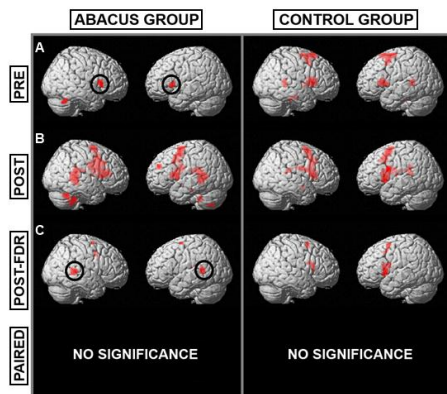
In the serial addition task, ABA group demonstrated significantly stronger decreased reaction time in comparison to CON group (ABA $p = 0.011 < 0.05$ and CON $p = 0.258$, 17.35% and 9.33% decrease respectively). ABA group also expressed a 15.87% decrease in anxiety to mathematic processing, while CON group expressed an 8.81% increase. In working memory expression, ABA group ($n = 21$) showed significant change ($p = 0.037 < 0.05$) and advanced 9.11 percentile on the WISC-IV exam's working memory subsection (from 81.19 to 90.30), and the effect size is medium (Cohen's $d = 0.43$). The CON group ($n = 22$) revealed no significant change ($p = 0.238$) and advanced 4.83 percentile (from 82.68 to 87.51) The ABA group expressed improvement in the letter-number sequencing subtest, making a 9.60% increase (9.43 to 10.33,) while the CON group made a 5.00% improvement (10.00 to 10.50.) However, the CON group demonstrated greater growth in the arithmetic subtest from 8.82 to 9.32, while the ABA group made a slight improvement from 9.43 to 9.71.

Table 3 - Summary of significant clusters of the two-sample paired T-test within the ABA group before and after AMC training intervention.

Anatomical location				Statistical values		
Region	x	y	z	Cluster size	t-Value	p-Value
Left inferior parietal lobule	-60	-36	33	124	6.10	< 0.001
	-60	-30	15		5.45	
	-57	-36	21		5.26	
Right inferior parietal lobule	63	-33	36	38	4.85	< 0.001

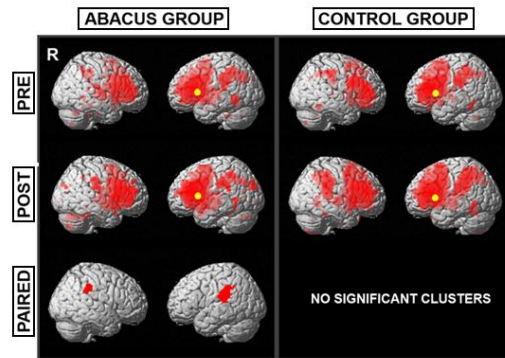
The functional connectivity seed was placed at the left Broca area ($x = -39$, $y = 24$, $z = 15$, radius = 5 mm.) The MNI coordinates and t-values correspond to the local maxima of the centers of voxel clusters. The statistical threshold was set at $p < 0.05$ using AlphaSim correction (with combination of threshold of $p < 0.001$ and minimum cluster size of 12 voxels.)

Figure 2 - General pattern of activity during the serial addition task for ABA and CON groups.



(A) Pre-intervention activity is mainly in the prefrontal region. (B) A general increase in post-intervention activity can be found. (C) When the within group analysis is performed with FDR correction, a shift in post-intervention activation to the parietal regions is suggested in the ABA group. However, no significance is found when two-sample paired t-test is performed. The statistical threshold was set at $p < 0.05$ using AlphaSim correction (with combination of threshold of $p < 0.001$ and minimum cluster size of 12 voxels,) and set at $p < 0.05$ using FDR correction.

Figure 3 - Resting-state functional connectivity findings.



The pattern of significant positive correlations between the left Broca area seed ($x = -39, y = 24, z = 15$, radius = 5 mm) and the fronto-parietal network is seen in both the ABA and CON groups. Significance in two-sample paired t-test indicates increased functional connectivity between LBA and bilateral inferior parietal lobules in the ABA group after AMC training intervention. The statistical threshold was set at $p < 0.05$ using FWE correction for the within group analyses and using AlphaSim correction (with combination of threshold of $p < 0.001$ and minimum cluster size of 12 voxels) for the two-sample paired t-test.

Discussion

In the past decade, several reports of AMC have demonstrated distinct brain activations differences between experts and novices (2-5). On functional MRI results, non-experts show activity in the prefrontal and perisylvian areas, while experts with long-term training show more activation over premotor and superior parietal regions. In recent years, structural and functional connectivity were deployed to study brain intrinsic integrity in children with 3-year training of the AMC (7,13). Increased integrity in white matter tracts were observed over right premotor cortex, corpus callosum, and left occipito-temporal junction. The findings also suggested long-term abacus training may improve working memory capacity (7). Resting state MRI (rsMRI) revealed enhanced connectivity between right supplementary motor area (SMA), and right inferior frontal gyrus (IFG), suggesting more extensive engagement of visuo-spatial-attention networks in trained subjects while performing numerical working memory task (13). Multiple cortices on functional MRI were involved, including IFG, SMA, posterior superior parietal gyrus (PSP), and superior occipital gyrus, and it implies the long-term abacus training effects could be transferred to the untrained working memory task.

Most past studies focus on cross-sectional analysis of abacus experts and non-experts, but neglect the potential midway paradigm shift (*paradigm drift*) within the relatively long time required to become an expert. But, how soon can we expect changes after initializing training on the functional level and the behavioral level? The Chinese Abacus Association in Taiwan states that in past experience, the initial

greatest level of behavioral improvement can be expected in training periods between six months to one year, implying functional changes may be in place before physical changes become detectable. Stigler's study in 1986 revealed children after one year AMC training could develop the ability of mental abacus (14). Irwing's report in 2008 suggested a general intelligence improvement after receiving only 34 weeks of abacus training (6). Therefore, we assume that 6 months is the minimum period required for the change.

Paradigm drift in mental calculation after abacus training

In the local Chinese and Japanese cultural background, speed and accuracy of mental calculation is crucial to daily life and an important aspect of academic success. The “number sense” greatly depends on the parietal, prefrontal, and cingulate areas, with the HIPS playing a key part in the manipulation of quantity (18). Neuroimaging studies revealed the activation of different neural pathways between untrained children mental calculation and trained experts: the mental calculation task in children mainly activate prefrontal and perisylvian zones of the left hemisphere, with differences shown while performing simple and complex calculation; in sharp contrast, when children are trained in AMC, the activation shifts focus to visuo-motor and visuo-spatial pathways. This is consistent with our knowledge of how AMC is trained in its steps: with each cognitive focus, a change in the underlying functional network can be witnessed in the end results.

With knowledge of the training methods and its end result reflected in neuroimaging, we ask ourselves: what changes can be expected in the relatively short-term training of six months? Research show functional differences between three-year experts and untrained subjects, physical properties can be expected to change after long-term training, and general improvements are noted in time as short as thirty-four weeks. But the greatest behavioral improvements are suggested within six months to one year of training, and we proposed the intrinsic functional circuits should rightfully reflect this change.

Past studies suggest a shift of activation from frontal lobes to parietal lobes was observed with the gain of arithmetic competence, and intra-parietal shift of activation from HIPS to angular gyrus were also reported (19). Evidence for developmental change in mental arithmetic revealed a shift of activations with ages from prefrontal cortex to left inferior parietal lobe. The increased functional specialization of left inferior parietal cortex in mental arithmetic was accompanied by decreased dependence on memory and attention resources with development (20).

Our results demonstrated shift in activation region consistent with our expectation along the fronto-parietal network, but not to the extent of further parietal regions, such as angular gyrus and posterior superior parietal cortex, as suggested by

studies involving long-term trained experts. We propose the current and eventual changes to follow a paradigm “*drift*” along the circuitry, beginning at the prefrontal sectors and moving gradually to the parietal. An increase in functional connectivity between LBA and the left inferior parietal gyrus shown in our rsMRI results suggest the circuitry improves after AMC training.

Our results also revealed a midpoint for this eventual shift that may provide deeper understanding into AMC training’s effect on the learning brain. But, what is the possible direction of future paradigm shift? PSP was proposed to be recruited for mental abacus (3,4), and the activations in angular gyrus increased with the gain of arithmetic knowledge (19). Therefore, we propose two different directions for end-term change: to shift cranially towards the horizontal intra-parietal sulcus (HIPS) and the posterior superior parietal region, or to shift dorsally towards the angular gyrus.

Working memory training

Working memory (WM) is one’s ability to keep limited information in queue and able to be manipulated over a short period of time. This specific cognitive ability is of crucial importance in many different cognitive skills or tasks, and improvement of WM capacity has been proven in several studies (8,21,22,23). WM training-related changes on brain activation were observed in frontal, parietal cortex and basal ganglia (21,22), and it was even proposed intrinsic brain activity and connectivity can be altered by cognitive training (8).

Improvement of implicit WM training can always be expected based on the repetitive training and adjustments of tasks. It is more important to evaluate the potential transfer of WM training to other non-trained tasks. The generalization of WM training effects to other non-trained tasks has been difficult (24,25), but there are promising studies demonstrating transfer after WM training to non-trained tasks can be achievable (22,23,26,27). In the current study, we rediscover a key element of Chinese culture, evaluate the validity and effectiveness of AMC training as a tool to augment WM capacity, and verify the possibility of training effect transfer to the untrained working memory test.

The effects of training in brain plasticity are undeniable, but the future focus should be for which training regimens may result in the best transfer effects, and to whom it is most beneficial (23). AMC training can be considered as an effective method of WM training with a time constraint. Despite its limitations and time-consuming training regimen, it provides stronger training results and retains higher transfer potential than conventional WM training. In modern era, with calculators that can be operated by the simplest of minds, we propose to view the abacus no longer as a tool for trade or computation, but as a toy to learn through play.

Conclusions and significance of the study

Within the relatively short (6 months) training of abacus-based mental calculation, significant changes were observed in fronto-parietal network and working memory behavioral expression. Functional connectivity analysis with rsMRI revealed increased connectivity between the left inferior frontal area and the inferior parietal lobe. Most importantly, the AMC training effect can be generalized to affect the untrained tasks of the WISC-IV exam's working memory subsection.

But are these effects persistent in the long run? And furthermore, what is the required amount of training before one completes the paradigm shift to “transform” into the mental model as that of experts? And even though the present study shows AMC training effects generalized to untrained working memory tasks, but there is still a long way to go before the leap is made to complex cognitive abilities such as reading, arithmetic, or general intelligence. We recommend future AMC-related studies place focus on the training conditions and target subjects most suitable to produce lasting effects on the mental scheme. Additionally, the evaluation of transfer effects should not be to general skill assessments involving multiple complex cognitive abilities but to specific cognitive traits.

In conclusion, this study offers reappraisal of the abacus, a traditional Chinese tool, and its training in the modern setting. Compared to the common practice of task repetition, AMC training is a more complex and interesting method of cognitive training with a stronger sense of self-accomplishment through its step-by-step training curriculum. Our results also suggested AMC training may increase learners' confidence in arithmetic tasks and alleviate anxiety. It has potentially long-term positive psychological effects in future learning. AMC is not only an arithmetic operation, but it is also an appropriate tool to improve working memory capabilities by exercising visuo-motor and visuo-spatial skills. With aid of educational neuroscience, we can take a new perspective on the traditional Chinese tool for calculation in the modern age.

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