Effects of a 12-month progressive physical and cognitive training program on occipital alpha-band power during a visual working memory task

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Aging is known to degenerate cognitive functions, but regular physical and cognitive activity operate as protective factors against the impairment. The purpose of this MEG experiment was to find out how a 12-month long structured progressive physical and cognitive training program affects on occipital alpha-band (8-13 Hz) power during a visual working memory task. Control group participants took part only in physical training program. This study is carried out as a part of PASSWORD research project in co-operation with Jyväskylä Centre for Interdisciplinary Brain Research, Department of Psychology and Gerontology Research Center of Faculty of Sport and Health Sciences, University of Jyväskylä. Altogether, 24 elderly completed the study, of which eight were male and sixteen were female. Healthy participants were born between the years 1935 and 1946 (mean year of birth 1942,5). Participants completed an in-house developed visual working memory task with modified Karolinska Directed Emotional Faces used as stimuli. The task contained a visual distractor between encoding and retrieval stimuli. During the first 1500 ms after distractor appearance alpha-band power seemed to vary in two phases, of which during the first alpha-band power decreased and during the second alpha-band power increased. Thus, inspection of the results was made in two time windows. No differences between the groups were found in either time window. However, the alpha power modulation in response to difficult distractors was found to be stronger than in response to easy distractors in both time windows. In addition, the first time window (300-800 ms) showed a decrease in alpha power (alpha desynchronization) especially in the right occipital hemisphere where the facial recognition areas are generally located. In the second time window (800-1500 ms) increase in alpha power (alpha synchronization) was discovered to be strongest in the left occipital hemisphere. Moreover, alpha-band power in left occipital areas decreased between the pre- and post- intervention measurement. Inspections of pre-planned contrasts without the group effects confirmed the observed trend that the alpha desynchronization effect in the first time window was mainly brought by right occipital hemisphere and the alpha synchronization effect in the second time window was mainly brought by left occipital hemisphere. The results suggest that a group participating in combined physical and cognitive training program did not differ from physical training group in occipital alpha-band power changes during a visual working memory task. The results further suggest that simultaneous retaining and inhibiting of different visual stimuli might happen sequentially and in interaction with both hemispheres. This study is a multidisciplinary brain research project of the University of Jyväskylä and it is funded by the Academy of Finland.

Key words: physical training, cognitive training, alpha rhythm, magnetoencephalography, MEG, inhibition, working memory, visual distractor, aging

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Ikääntymisen tiedetään heikentävän kognitiivista prosessointia, mutta säännöllinen fyysinen ja kognitiivinen aktiivisuus toimivat suojatekijöinä ikääntymisen aiheuttamia kognitiivisia muutoksia vastaan. Tämän tutkimuksen tarkoituksena oli selvittää, kuinka 12 kuukauden mittainen kognitiivisen ja fyysisen harjoittelun ohjelma vaikuttaa tutkittavien okkipitaalilohkon alfaoskillaation (8-13 Hz) modulaatioon visuaalisen työmuistitehtävän aikana. Tutkimuksen kontrolliryhmä osallistui ainoastaan fyysisen harjoittelun interventioon. Tutkimus on toteutettu osana laajempaa PASSWORD-tutkimusaineistoa yhteistyössä Jyväskylän yliopiston Monitieteisen Aivotutkimuskeskuksen, Gerontologian tutkimuskeskuksen ja Psykologian laitoksen kanssa. Yhteensä tutkimukseen osallistui 24 tutkittavaa, kahdeksan miestä ja 16 naista. Tutkittavat olivat perusterveitä, ja syntyneet vuosina 1935-1946 (ka. 1942,5). Tutkittavat suorittivat visuaalisen työmuistitehtävän, jonka ärsykkeinä käytettiin neutralisoituja Karolinska Directed Emotional Faces -kasvokuvia. Työmuistitehtävän aikana tutkittaville esitettiin visuaalinen distraktori ensimmäisen ärsykkeen ja mieleenpalautuskuvan välisenä ajanjaksona. Ensimmäisen 1500 ms ajan distraktorin ilmenemisen jälkeen alfarytmin amplitudi vaihteli kahdessa syklissä, joista ensimmäisen aikana alfarytmin voimakkuus laski ja toisen aikana alfarytmin voimakkuus nousi. Täten jatkotarkastelut toteutettiin kahdessa eri aikaikkunassa. Koe- ja kontrolliryhmän välisiä eroja ei löytynyt kummassakaan aikaikkunassa. Kuitenkin, alfarytmin modulaatio vasteena vaikeisiin distraktoreihin oli voimakkaampaa kuin vasteena helppoihin distraktoreihin molemmissa aikaikkunoissa. Lisäksi ensimmäisestä aikaikkunasta (300-800 ms) oli löydettävissä alfarytmin desynkronisaatiota oikean okkipitaalilohkon alueilta, joissa visuaaliset kasvojentunnistusalueet yleensä sijaitsevat. Sen sijaan toisessa aikaikkunassa (800-1500 ms) alfarytmin synkronisaatio oli voimakkainta vasemman okkipitaalilohkon alueilla. Tämän lisäksi alfarytmin voimakkuus vasemman okkipitaalilohkon alueilla laski alku- ja loppumittauksen välillä. Ilman ryhmävaikutuksia toteutetut parittaisten t-testien vertailut vahvistivat havaittua suuntausta, jonka mukaan alfarytmin voimakkuuden lasku (desynkronisaatio) ensimmäisessä aikaikkunassa on pääosin oikean okkipitaalilohkon alueilla tapahtuvaa, ja toisen aikaikkunan alfarytmin voimakkuuden nousu (synkronisaatio) pääosin vasemman okkipitaalilohkon alueilla tapahtuvaa. Tuloksien mukaan yhdistetty kognitiivisen ja fyysisen harjoittelun ryhmä ja ainoastaan fyysiseen harjoitteluun osallistunut ryhmä eivät eronneet toisistaan visuaalisen työmuistitehtävän aikaisissa okkipitaalilohkon alfarytmin voimakkuuden muutoksissa. Lisäksi tulokset viittaavat siihen, että useamman visuaalisen ärsykkeen samanaikainen aktiivinen prosessointi ja inhibitio tapahtunee peräkkäin ja vuorovaikutuksessa molempien aivopuoliskojen kanssa. Tämä tutkimus kuuluu Jyväskylän yliopiston profilointialaan monitieteinen aivotutkimus, jota rahoittaa Suomen Akatemia.

Avainsanat: fyysinen harjoittelu, kognitiivinen harjoittelu, alfarytmi, magnetoenkefalografia, MEG, inhibitio, työmuisti, visuaalinen distraktori, ikääntyminen

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Introduction

Many physical and cognitive functions degenerate with aging. The majority of fundamental cognitive processes, such as reasoning, memory, perception and learning are affected by cognitive aging. Degeneration of cognitive functions can be interpreted to an outgrowth of aging-related structural changes in the brain, such as neuronal cell loss, cerebral ventricles expansive growth and brain tissue atrophy (Kemper, 1994) and the changes seem to be centered around prefrontal cortex, there affecting especially to gray matter volume (Peters, 2006; Trollor & Valenzuela, 2001). Additionally, aging seems to be in a relation with subcortical white matter volume changes and hyperintensities (WMH) which at least partly affect cognitive impairment due to aging (Almkvist, Wahlund, Andersson-Lundman, Basun & Backman, 1992). As a result of simultaneous degeneration of cognitive and physical functions, the elderly suffering from these diminutions are more likely to perform poorly in tasks which require concurrent physical and cognitive performance.

At the same time, the age structure of the population in European countries is going through a period of change. Life expectancy grows continuously, and also men are catching females up. According to the Statistics Finland (2019), the average life expectancy of Finnish population increased by over 5 years between the years 1996 and 2016 and it still continues growing. As a result, the elderly people have more years after retirement. In consequence of increased after-retirement leisure time, individual competence and social capital which have been grown during career paths, could be invested in projects of individuals’ own interest. However, this requires that individuals after retirement manage to maintain their cognitive and physical capabilities. The scholars of the area term this comprehensive phenomenon successful aging, and it seems to be connected, above all, to obeying a healthy lifestyle.

Acknowledging the importance of successful aging for the society, it is no wonder that neural and cognitive components of aging are widely attracted by researchers of the field. For instance, seeking publications studying the relation of physical activity and cognition, samples of elderly people are highlighted (see Etnier, 2008; Colcombe & Kramer, 2003). However, the relation between aging and cognition has been under interest far more longer: since the mid-1960s, the effects of aging on different cognitive components have been studied using many different cognitive metrics and experimental settings. This research has mainly been guided by two research directions: one has been focusing on separating the components of cognitive performance which degenerate with aging and gaining more understanding on which stage of a life-span these changes in each component typically most considerably manifest, and the other's more cognitive neuroscientific emphasis has been in absorbing in occurrences of aging-related cognitive changes in brain function and structure (Anderson & Craik, 2016). The latter has naturally gained a foothold in the research over the latest decades as emerging neuroimaging techniques have enabled wider use of functional experimental methods in neuroscience research.

In addition, non-clinical studies of successful aging, which have attracted broad attention in recent years, could be distinguished in its own wave of research. Common to these studies is studying the individual characteristics and protective factors of healthy elderly peoples' cognitive trajectories who tend to averagely perform better than the same cohort control group in cognitive assessment tasks. These studies have indicated that stable aging and declining aging groups' modifiable risk factors and memory trajectories differ from each other (McFall, McDermott & Dixon, 2019). In their latest review, Dixon and Lachman (2019) comprehensively list protective factors of cognitive decline in aging, naming such factors as education, regular physical activity, high social support, sufficient amount of sleep, cognitive activity and individual attitudes and beliefs about aging. A review of Klimova, Valis and Kuca (2017) identifies most of the above-mentioned risk factors and adds an adherence to Mediterranean dietary habits to the list. However, Dixon and Lachman emphasize that noted protective factors of cognitive decline have often bidirectional mechanisms of influence to one's health, meaning that most of the protective factors and risk factors are substantially the same. This means that, for instance, the protection of a cognitively challenging career can in the second case turn into a risk if cognitive load in the individual's workplace has not occurred regularly, or on the contrary, work-related cognitive stress has been intense and continuous.

However, all the identified risk and protective factors are not under the influence of individual choices. The factors affecting cognitive performance are divided into modifiable and non-modifiable risk factors, and bidirectional influence relation encompasses only a category of modifiable risk factors. Twin research has shown that approximately 40 percent of the total variance in cognitive abilities may be considered to belong to the modifiable factors group (McClearn, 1997). Although modifiable factors account for relatively small portion of the total, it is the very sector that people can influence with their own actions. Thus, apart from being able to successfully diagnose the aging-related mild cognitive impairment and progressive memory disorders, it is important to look more closely at the modifiable factors that support successful aging and provide people evidence-based information of maintaining their health.

With this study, it is aimed to determine practices supporting successful aging by studying the brain basis of inhibition and cognitive capacity of healthy elderly and examine its association with cognitive and physical training interventions, both of which are considered to be protective factors of cognitive aging when exercised regularly. Furthermore, it is aimed to discover whether simultaneous participating in cognitive and physical exercise interventions accelerates the brain-level intervention effect of inhibiting irrelevant stimuli during a visual working memory task compared to those who only participate in the physical exercise intervention.

Aging and cognition

The studies of cognitive aging and intelligence have already long made a segregation between two concepts of cognition: crystallized and fluid intelligence (Cattell, 1963). Crystallized intelligence contains a large number of cognitive, partially long-term memory dependent functions that develop with age and maturation, such as deductive reasoning competence and general knowledge. A concept more closely interfaced with acute information processing, fluid intelligence, contains features such as inductive reasoning competence, processing speed and creative problem solving. Several studies have suggested that fluid intelligence is more sensitive to changes caused by aging compared to crystallized intelligence and age-related changes in fluid intelligence begin to manifest in an earlier stage than changes in crystallized intelligence (Horn, 1982; Kaufman & Horn, 1996). As components of fluid intelligence rely heavily on an individual’s competence of acute information processing, the major focus of research about preventing aging-related decline has been on processes of memory and attention.

Since working memory functions decline with aging (Chen, Hale & Myerson, 2003; Peich, Husain & Bays, 2013) and aging also causes harm to processing speed, accuracy and comprehension (Weeks & Hasher, 2013), elderly people are generally at disadvantage in processing tasks that require speed and accuracy. Due to the generic nature of working memory, its decline tends to affect negatively to the other cognitive processes as well. On the other hand, conscious learning is hardly possible without efficient attention. Thus, it is possible that the signs of cognitive aging appearing as problems in processing tasks' phases of encoding and retrieval are the result of a decline in top-down attentional control (Mok et al., 2016).

According to Dempster (1992), aging-related cognitive impairment would partly result from a decrease of an inhibitory capacity to suppress non-task-relevant external stimuli or internal associations. The ability to suppress extrinsic, irrelevant stimuli is largely controlled by the frontal cortex, which is known to be the first brain areas that deteriorate with old age. As a result, the effect of aging is most evident in these areas. An ERP study of Zanto, Toy and Gazzaley (2010) supports Dempster's observations by noting that the effectiveness of inhibiting the irrelevant visual stimulus could be dependent on the stimulus being suppressed. This means that stimuli with more complex visual information, such as human faces, could be more challenging to inhibit due to age-related decline compared to stimuli with more simple features, such as plain colors. However, the hypothesis of age-related inhibitory deficit should not solely be overplayed. ERP studies have provided indications that both inhibitory deficit and information processing decline are acting in conjunction behind the aging-related changes (Gazzaley et al., 2008).

Cognition and physical activity

There has been a substantial amount of reports on the positive health effects of committing oneself to a physically active lifestyle. According to a comprehensive listing of Zoeller (2010), the positive effects of regular exercise and physical activity can be found on, among other things, individual life expectancy, skeletal muscle power output, mineral density of bones and cardiovascular disease prevention. Furthermore, health effects of the elderly's regular physical activity extend to the cognitive performance. Studies of cognition and physical activity made with the elderly indicate that larger amount of regular physical activity at least maintains, but can even improve cognitive function, and increasing the activity by an old age may especially improve executive functions (Zoeller, 2010).

In combined cognitive and physical training interventions, particularly participants with low baseline level have benefited from training (Kalbe et al., 2018).

Multiple cross-sectional design studies provide correlational evidence of the relationship of the amount of physical activity and enhanced cognitive performance, particularly in the groups of elderly people (Christensen & Mackinnon, 1993; Spirduso, MacRae, Macrae, Prewitt & Osborne, 1988). However, issues arising from correlational relationships have been partially resolved afterwards. Since the turn of the millennium, there have been several massive follow-up studies and meta-analyses of thousands of subjects and many years which have supported the protective connection of regular physical activity on age-related cognitive impairment.

Prospective study of Lytle, Vander Bilt, Pandav, Dodge & Ganguli (2004) conducted a two-year follow-up study on over a thousand US people over 65 years of age studying the connections of physical exercise type, frequency and duration on global cognitive function, and found that the higher level of exercise was in association with lack of cognitive impairment during the follow-up period. And further, six-year follow-up study of Yaffe, Barnes, Nevitt, Lui & Covinsky (2001) with more influential research data studied over 5900 white US female and found that greater involvement to moderate-to-vigorous physical activity reduced the risk of experiencing cognitive decline during the six-year follow-up. Moreover, it is noteworthy that most of the follow-up studies, like the two above, use Mini-Mental State Examination test (MMSE) as a measure of age-related cognitive impairment, which is known to be a fairly robust measure of cognitive impairment. Thus, it seems safe to state that, based on research, regular physical activity protects the elderly from cognitive impairment.

However, due to the breadth of the concept of cognition, the effects of exercise and physical activity on the components of cognition may still need to be specified. A comparative study of Shay and Roth (1992) examined differences of high aerobic fitness and low aerobic fitness subjects on several different neuropsychological test results and found that between-group fitness differences of the elderly subjects became significant in the tests that require processing or reproducing of visuospatial information. If high aerobic fitness can be assumed as a consequence of participating in regular physical activity, it could also be assumed that the effects of physical activity on the elderly are particularly evident in visuospatial processing tasks. On the other hand, Zhu et al. (2017) observed that greater amount of objectively accelerometer-measured moderate-to-vigorous physical activity on the elderly had a positive effect on the executive function and working memory. The findings of extensive review by Hayes, Hayes, Cadden and Verfaellie (2013) support the above by discovering that aerobic fitness on the elderly is associated with higher volume in brain areas which are related to executive functions: cingulate cortex, lateral prefrontal cortex and lateral parietal cortex. Thus, it seems that different forms of exercise and physical activity might have various effects and influence mechanisms on cognition.

Physical activity and brain

When the relationship of regular physical activity and aging-related cognitive impairment is examined, it is also essential to acknowledge the exercise-induced neurobiological responses behind the changes of cognitive performance. One of the most important mechanisms which produce cognitive changes are structural changes in neural networks which, among other things, include growth in hippocampal volume (Erickson et al., 2011) and gray matter volume in general (Benedict et al., 2013). Exercise-induced hippocampal volume growth has indicated to be an outgrowth of the brain-derived neurotrophic factor (BDNF) mediated neurogenesis in hippocampal areas, especially in the dentate gyrus granule cells (Brown et al., 2003; Liu & Nusslock, 2018), which is strongly linked to the activity and performance of long-term memory functions. Additionally, physical exercise seems to cause an increase in cerebral blood volume (CBV) in the dentate gyrus on both rodents and humans, which is also indicated to correlate with cognitive performance (Pereira et al., 2007). Rosenzweig and Bennett (1996) reviewed other exercise-induced structural changes in rodent cerebral cortex and discovered increased number of dendritic spines and branches along with growth of cortical thickness. In addition, regular exercise on aged rodents has been discovered to increase the synaptogenesis, number and size of synapses in cerebral cortex (Van Praag, Shubert, Zhao & Gage, 2005).

In summary, on the structural changes caused by exercise training in rodents and humans could be noted that the changes seem to support a more efficient and better organized central nervous system activation. And further, as a result of better organized nervous activation could be thought that tasks requiring acres of cognitive capacity could be performed more flexibly and with a smaller effort. One of the most considerable underlying mechanisms of more organized nervous activation found on rodents and humans is long-term potentiation LTP (Farmer et al., 2004), which makes consolidation more efficient by increasing hippocampal neurons sensitivity of nerve impulse transmission from other neurons.

In addition to the structural changes caused by aging, there are functional changes in the brain which must be considered. The focus of research on exercise and functional changes has mainly concentrated on neurotrophins, neurotransmitters and blood circulation. According to the current research, the major protein of growth factors in neurotrophin family is neurogenesis mediating BDNF. Levels of BDNF have been found to increase in response to exercise both in rodents and in the human brain, and in addition, the magnitude of BDNF release has been found to correlate with exercise intensity (Ferris, Williams & Shen, 2007). Positive correlation between BDNF level and physical training has recently found also in a study with elderly subjects (Küster et al., 2017).

As a result of aging, changes also occur in the generation of neurotransmitters. Synthesis of dopamine, a transmitter associated with e.g. Parkinson's disease, seems to be influenced by aging (Berry et al., 2016). However, it was recently found that physical activity seems to facilitate dopamine transporter binding on elderly people (Shih, Moore, Browner, Sklerov & Dayan, 2019). In addition to dopamine, physical exercise also seems to influence the function of serotonergic and noradrenergic systems (Chaouloff, 1989).

Alpha-band oscillation

Brain oscillations are rhythmic, recurrent and sinusoid waves of neuronal activity in the central nervous system. In practice, brain rhythmic waves of different frequencies mean that neuronal populations of brain network fire at different rates. Oscillations also appear in various forms during different sensory input and internal states depending on the triggering frequency of the nerve cell population required for ongoing operation. Thus, studying oscillations utilizing brain imaging techniques is a convenient manner to discover the power and course of activation in different parts of the cerebral cortex during a certain task. One of the striking features of alpha oscillation is its considerable decrease in amplitude in response to eye opening (Bazanova & Vernon, 2014), known as desynchronization. Partly because of this historical observation, it has traditionally been thought that alpha oscillation would be primarily a cortical idling rhythm that is strongly associated with rest and lack of cognitive load.

However, increasing research has at least partially refuted the claim of alpha's primary role in cortical idling, and current interpretation is that alpha rhythm has many functional purposes in human psychophysiology. One of the functions associated with the alpha rhythm is the inhibition of stimuli irrelevant to the current task. Jensen and Mazaheri (2010) hypothesize that the primary role of alpha rhythm would be functional inhibition by targeting the active inhibition to cortical regions that are not relevant to the ongoing cognitive performance. Thus, alpha does not passively give way when exiting the cortical idling, but actively avoids the areas essential for processing to inhibit irrelevant cortical areas and enhancing the capacity of processing. This hypothesis is supported by current human EEG covert attention research, whereby conscious shifting of attention to the other side of the field of vision causes a decrease in alpha rhythm activity in the contralateral cortical areas which are mainly responsible for processing the stimuli presented in the areas of attention (Rihs, Michel & Thut, 2007).

A review of Klimesch, Sauseng and Hanslmayr (2007) discussed of alpha-band modulation during working memory tasks and noted that the increase in alpha power occurs particularly during the working memory retention interval, when stimuli to be remembered must be actively processed in working memory. Although there is ample evidence of alpha's contribution in the inhibition hypothesis, only few studies have focused on alpha's function on distractor inhibition. One of the most essential differences between distractor inhibition and functional inhibition is that the distractor tasks are designed to burden the function of brain areas and neuronal pathways responsible for ongoing task, whereas functional inhibition can be assumed as alpha's ability to suppress the function of brain areas not responsible for processing material relevant to a specific task.

Recently published study of Schroeder, Ball and Busch (2018) investigated alpha's role in distractor inhibition during working memory task maintenance interval with easy and difficult distractors, and the results showed that difficult distractors during memory retention phase caused alpha desynchronization. As alpha power decrease is generally assumed to signal more efficient processing and neuronal excitation, the results could indicate that alpha's role in inhibition would mainly target to brain areas non-critical for ongoing task. However, there are still contradictions about alpha's role in distractor inhibition, so further research is needed especially with samples consisting of the elderly, because the function of inhibition and attentional capacity is critical for successful aging.

Aims of the study

This study aims to investigate the effects of a 12-month long structured and progressive physical and cognitive training program on the brain basis of inhibition in a visual working memory task performed with magnetoencephalography. The focus of the study is on occipital alpha oscillation power changes during distractor inhibition processes of visual working memory task retention phase. To answer the questions that arose from the earlier research of the field, our research objectives formed as follows:

The primary objective of the study is to investigate whether cognitive training enhances the change in inhibition caused by physical training, both known to act as protective factors against aging-related cognitive impairment. In other words, the primary objective of the study is to investigate between-group differences of physical training group's (PT) and physical and cognitive training group's (PTCT) occipital alpha power changes during two times of measurement (pre and post) in response to easy and difficult visual distractors. The secondary object of the study is to investigate whether the power of inhibition in alpha-frequency depends on the visual complexity of the distractor picture. In other words, the secondary object of the study is to investigate averaged alpha power modulation differences in response to easy and difficult distractors regardless of the intervention groups.

The hypotheses concerning the research objectives were set in tandem with earlier, though partially restricted, knowledge of the field as follows:

Combined physical and cognitive training results in greater change in alpha power than plain exercise training regardless of visual distractor difficulty.

In both times of measurement, alpha power change is greater in response to difficult visual distractors than easy visual distractors.

Methods

The research data of this master's thesis is gathered as a part of the PASSWORD study project. The PASSWORD study is carried out in collaboration with University of Jyväskylä's Department of Psychology, Gerontology Research Center of Faculty of Sport and Health Sciences and Jyväskylä

Centre for Interdisciplinary Brain Research between the years 2018 and 2019. The main objective of the study project is to study the effects of 12-months-long combined physical and cognitive training program on the walking speed and cognitive skills of elderly men and women. The physical training intervention, comprising individually targeted progressive supervised training sessions and home exercises, lasted for 12 months. Half of the participants took also part in the cognitive computer-based training targeting working memory and different components of executive functions. A proportion of the PASSWORD study subjects were randomized into PASSWORD BRAIN sub-study which studied the combined effects of physical and cognitive training interventions on attention-specific sensory and cognitive processes by using MEG recordings.

Participants

This study is a parallel group single blinded randomized controlled trial with two research arms; Physical Training (PT, control) and a combination of Physical and Cognitive Training (PTCT). The subjects were from 70 to 85 years old and they were recruited from Jyväskylä area. The inclusion criteria comprised being able to walk at least 500 meters without assistance, sedentary or at most moderately physically active lifestyle (less than 150 minutes walking per week and no regular attendance in strength or power training) and ≥24 points in Mini Mental State Examination test (Sipilä et al., 2018). Altogether 310 participants were recruited of which 155 were randomized into physical training (PT) group and 155 into physical and cognitive training (PTCT) group after baseline measurements. Again, 28 participants (14 PT, 14 PTCT) took part in the PASSWORD BRAIN sub-study which, in addition to above-mentioned groups' exercise sessions, included three MEG recording sessions, one at the baseline, one during the 6-month and one at the 12-month follow-up. The data of this master's thesis consists of the first (baseline) and the last (12-month follow-up) measurement results of twenty-four PASSWORD BRAIN study participants who completed the all three MEG recordings. Participants were born between the years 1935 and 1946 (mean age 75,3 years, range 72-83 years). Eight of the participants were male and sixteen were female. Four of the participants dropped out before the 12-month MEG recording, two of the drop-outers were males and the other two females. All the drop-outers were participants of a PTCT group. PTCT group participants (n=10) were from 72 to 78 years old (mean age 74 years) and PT group participants (n=14) were from 72 to 83 years old (mean age 76,4 years).

Interventions

12-month-long intervention's progressive exercises were partly supervised and partly self-directed home exercises. The supervised sessions aimed to the maximal improvement effects as the self-directed home exercises facilitated the adaptation to an active way of life. Intensity, resistance, difficulty and number of training sessions were increased during the intervention. Participants' training adherence was monitored, and a diary of home exercises was kept on a daily basis.

The physical training (PT) intervention consisted of progressive resistance and balance training and aerobic physical exercises, mostly nordic walking. Physical training intervention was divided into six progressive periods varying in training volume, intensity and specificity. Each participant attended once a week to a supervised walking session which was performed outdoors. The objective intensity of nordic walking exercises was 13 (moderate) on the Borg scale and the duration and distance of walking sessions was monitored. The duration of walking sessions increased towards the end of the intervention. Supervised resistance and balance training sessions were held together and organized specifically in two senior gyms equipped by HUR resistance training machines which store performed sets, reps, and load of each workout. Each workout session included a period of balance training followed by resistance training aiming to improve the strength and power of lower extremity muscles. Each resistance training session included 8 to 9 different exercises for upper, lower and trunk body muscles and the core of the resistance training consisted of leg press, leg extension and leg curl exercises. For the core exercises, six-repetition maximum tests were organized during the first training period and after the third and fifth period to quantify the training load and to observe the progress. More detailed information of the physical training intervention methods is illustrated in *Table 1*.

The cognitive computer-based training (CT) program is an in-house developed web-based computer program targeting to prevent cognitive impairment by training working memory and different components of executive functions sensitive to mild cognitive impairment of aging. Altogether eight different cognitive tasks were selected into the training program, of which four different tasks are completed during each training session. The tasks were divided in two blocks which took turns between the sessions. The first block included tasks of letter updating, predictable set-shifting, spatial working memory maintenance and Stroop color tasks (inhibition). The second one included tasks of spatial updating, unpredictable set-shifting, spatial working memory maintenance, and Stroop number tasks (inhibition). The targeted frequency of cognitive training was from three to four times a week. However, during the first month of intervention only physical training sessions were organized, to engage participants better to the intervention. Participants were advised to complete the tasks as quickly and accurately as possible and duration of one training session was approximately 20 minutes. Those who had a computer at home were completing the same tasks as home exercises, and those who not, were offered locations equipped with computers to complete the home exercises. As well in PT, task difficulty increased towards the end of the intervention. Both of the interventions are summarized in *Table 2*.

Table 1. *Description of the multicomponent physical training intervention of the PASSWORD – study.*

Time, months	Programs/ RM tests	Supervised resistance/balance exercise program	Supervised walking/balance exercise program	Home gymnastic program
1-2	6 RM tests	Familiarization with equipment; RM for Leg press, Leg curl, Leg extension	150 min of aerobic exercise/week. Outdoors activities are encouraged throughout the intervention	
	Period 1 (adoption phase)	Warm-up with balance exercises; Resistance training at 50% of 1 RM, 2 × 20 reps (adoption phase)	Warm-up (walk at habitual speed and dynamic balance exercises while walking); 10-min continuous walk with RPE 13	Strength exercises for lower limb muscles; Postural balance exercise; Stretching exercises for major muscle groups
3-4	Period 2	Warm-up with balance exercises; Resistance training: resistance at 60% 1 RM, 2 × 15 reps	Warm-up (at habitual speed, dynamic balance exercises of increasing difficulty over time while walking); 10–15 min continuous walking with RPE 13	Strength exercises for lower limb muscles; Postural balance exercise; Stretching exercises for major muscle groups
5-6	Period 3	Warm-up with balance exercises; Power training: Resistance 50% 1 RM, 3 × 5 reps (fast contractions) Hypertrophy: Resistance 70% 1RM, 2 × 10 reps (resistance is increased by 1–2 kg if predefined number of reps is exceeded)	Warm-up (as in periods 3–4); 15–20-min continuous walk with RPE 13	Strength exercises for lower limb muscles with red TheraBand CLX; Postural balance exercise; Stretching exercises for major muscle groups
	6 RM tests	Leg press, Leg curl, Leg extension Agility training for two weeks	1 month break during summertime	
7-8	Period 4	Warm-up with balance exercises; Hypertrophy: Resistance training at 70% 1 RM, 3 × 10 reps (resistance is increased by 1–2 kg if predefined number of reps is exceeded)	Warm-up (as in periods 3–4) 20-min continuous walk with RPE 13	Strength exercises for lower limb muscles with green/blue Thera Band CLX; Postural balance exercise; Stretching exercises for major muscle groups
9-10	Period 5	Warm-up with balance exercises; Hypertrophy: Resistance 80%, 1–2 × 10 reps (resistance is increased by 1–2 kg if predefined number of reps is exceeded) Power: Resistance 60%, 1–2 × 6–8 (fast contractions)	Warm-up (as in periods 3–4); 20-min continuous walk with RPE 13 or 20-min walk with < 1 min intervals with RPE 15	Strength exercises for lower limb muscles with blue TheraBand CLX; Postural balance exercise; Stretching exercises for major muscle groups
	6RM tests	Leg press, Leg curl, Leg extension		
11-12	Period 6	Warm-up with balance exercises; Power: Resistance 60%, 3 × 6 reps (fast contractions) Hypertrophy: Resistance 80%, 2 × 10 reps (resistance is increased by 1–2 kg if predefined number of reps is exceeded)	Warm-up (as in periods 3–4); 20-min walk with < 1 min intervals with RPE 15	Strength exercises for lower limb muscles with blue TheraBand CLX; Postural balance exercise; Stretching exercises for major muscle groups

Note. Reproduced from Sipilä et al. (2018).

Table 2. *Summary of interventions.*

Intervention/Months	1	2-4	5-7	8-10	11-12
Physical training (PT) Supervised sessions, fr/wk Activity, duration	1 GYM:BT+ST	2 1 GYM: BT+ST 1 Nordic walk: 20min	2 1 GYM: BT+ST 1 Nordic walk: 30min	2 1 GYM: BT+ST 1 Nordic walk: 30min	2 1 GYM: BT+ST 1 Nordic walk: 40min
Home exercises, activity, duration	Walk: 60min spread over the week	BT+ST exercises Walk: 60-80min spread over the week	BT+ST exercises Walk: 80-100min spread over the week	BT+ST exercises Walk: 120min spread over the week	BT+ST exercises Walk: 110-120min spread over the week
Cognitive training (CT) Supervised sessions, fr/wk Effective duration	-	1 10-15min	1-2 15min	2 15-20min	2 15-20min
Home exercises, fr/week Duration	-	1-2 10-15min	2 15-20min	2 15-20min	2 15-20min

BT=Balance training, ST=Strength/Power training. BT and ST exercises were performed during the same session.

MEG recordings and procedure

All the MEG recordings of the study were completed in the MEG laboratory of University of Jyväskylä's Centre for Interdisciplinary Brain Research during the years 2018 and 2019. MEG recordings consisted of three MEG recording sessions, one at the baseline, one at the 6-month- and one at the 12-month follow-up. In this study, results from the first and the third measurements were used as data. The procedure of MEG recordings was controlled to be uniform for all the subjects. Empty room MEG recordings of two minutes were recorded before and after recording of an individual subject to monitor the magnetic interference level and to confirm irreproachable function of the system. Each subject's clothes and body were secured to be magnetic-free by investigating the noise level caused by a subject before beginning the actual recording. Magnetic-free clothes were offered to the participants in case of subjects' clothing was causing noise. Subjects suffering from presbyopia were offered magnetic-free pair of glasses to be used in the MEG room during the recordings.

MEG data was collected using a 306-channel (102 magnetometers, 204 planar gradiometers) whole-head Elekta Neuromag TRIUX® magnetoencephalography system (Elekta Oy, Finland) in a magnetically shielded room (VacuumSchmelze GmbH, Germany). The data was recorded with a 1000 Hz sampling frequency, a low-pass anti-aliasing filter of 330 Hz and a high-pass filter of 0.03 Hz. To ensure optimal quality of MEG data, general data acquisition set-up consisted of head position indicator (HPI) coils and 3D-digitized head tracking, electro-oculography (EOG) electrodes and electrocardiography (ECG) electrodes.

Subjects' scalp shapes and position of the HPI coils were digitized using Polhemus Fastrak 3D Digitizer and Quad Sensor Motion Tracker (Polhemus, VT, USA.) Head position of subjects was constantly monitored by five head position indicator coils attached to the scalp, two on the temples, two behind the ears and one on the upper forehead. Electro-oculography (EOG) was recorded using four electrodes, one lateral to each eye to detect horizontal eye movements and one above and below the right eye to detect eye blinks. In addition, subjects' ECG's were recorded to facilitate subsequent heart activity related artifact removal.

Both of the measurement sessions were following the same course of measurement. First, the subjects were seated into the MEG machine so that the top of their head were touching the MEG helmet surface. Thereafter, a resting state recording was measured for four minutes with eyes closed and four minutes with eyes open for data baseline in the absence of stimuli. Before starting the actual visual working memory and inhibition task, each subject practiced the task for a few trials to ensure that the subjects had internalized the task requirements. The stimuli were presented through an LED screen which was positioned approximately one meter in front of the MEG chair. Response controller was placed on a laptop table between the MEG chair and the LED screen.

Visual working memory task

The visual working memory and inhibition task consisted of 240 trials of Karolinska Directed Emotional Faces (Lundqvist, Flykt & Öhman, 1998), which were modified to be as neutral as possible in all the other features but facial characteristics. The modification was made by removing faces' hair and hairlines, and other specific identifiable features outside the face area to make the visual value of all stimuli equal. The KDEF pictures' facial expressions were neutral in appearance. Every trial consisted of encoding facial picture, a visual distractor picture and a retrieval facial picture. Overall, 120 of shown encoding and retrieval pictures were female faces and 120 were male faces, which all were unfamiliar to the subjects. The subjects were instructed to identify if the retrieval facial picture was same or different as the encoding facial picture and press the controller accordingly. The visual distractor pictures were divided into two categories, easy and difficult distractors. Facial KDEF pictures of a different person representing same sex acted as difficult distractor stimuli and easy distractor stimuli were facial-shaped blurred grey pictures of which it was not possible to detect facial features. Overall, 120 of shown visual distractors were easy and 120 were difficult. The trials were divided to four blocks of 60 trials, and subjects were offered a possibility to have a short rest of 1-2 minutes between the blocks to support their performance and attention maintenance.

In the beginning of each trial subjects were shown 1000 ms of grey fixation cross in the middle of the LED screen. The cross was followed by an encoding picture which was presented for 500 ms. After the encoding picture, the fixation cross was shown to the subjects for 2000 ms. The second cross was followed by either easy or difficult visual distractor which in both cases were presented for 500 ms. After the distractor, the fixation cross returned to the screen for 1000 ms. Next, a retrieval picture was shown to the subjects for 500 ms. The last visual component of a trial was an interrogation mark which was presented for 2000 ms, and during this time subjects had to decide whether the retrieval picture face was similar or different from the encoding picture. The structure of the task with an easy visual distractor is illustrated in *Figure 1* and the structure of the task with a difficult visual distractor is illustrated in *Figure 2.*

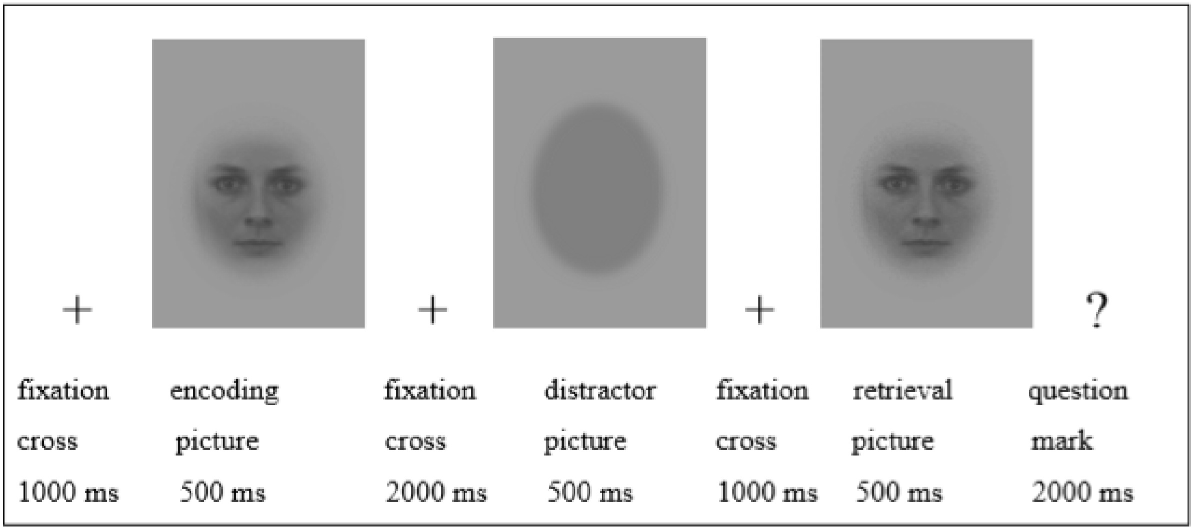

Figure 1. *Working memory and inhibition task with easy visual distractor.*

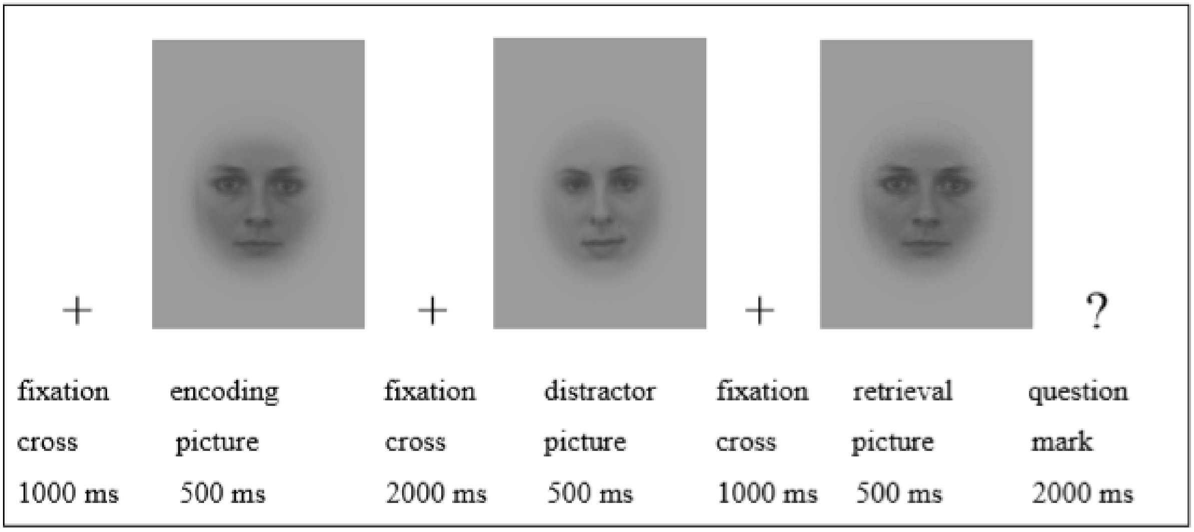

Figure 2. *Working memory and inhibition task with difficult visual distractor.*

MEG data processing

After the completion of the data acquisition, MEG data was processed with Elekta Neuromag MaxFilter 3.0 software program. Maxwell filtering is a data preprocessing program that utilizes Signal Space Separation algorithm to inhibit magnetic interference coming from inside and outside of the MEG sensor array, to suppress measurement noise and artifacts and to transform data between different head positions. All the data analyses after MaxFiltering were completed with Meggie. Meggie is an in-house developed MNE Python based software for analyzing MEG data with multiple possibilities for visualizing results of processing steps and final outputs (see Gramfort et al., 2013).

Cleaning the MaxFilter-processed MEG data from cardiac artifacts and interference causing eye blinks was made by independent component analysis (ICA). Artifact suppressed data was epoched to 4800 millisecond stretches determining the appearance of a distractor as a zero point. Epochs were extracted from 2400 ms prior to distractor appearance to 2400 ms after distractor appearance and it was done separately for each participant and for easy and difficult distractor picture. After extracting the epochs, averages were calculated separately for each type of distractor for each individual. Sequentially, time-frequency representations (TFRs) were calculated for each participant and distractor in both groups. Moreover, temporal spectral evolution (TSE) was applied to display alpha-band frequency oscillatory changes over time by isolating the power waveform for specific frequency band. For this purpose, a 4-Hz low-pass filter was employed to downsample the signal to meet with alpha-band amplitude. For statistical analysis of the data, numerical values of data for each subject were tabulated by hemisphere, measurement time, distractor type and group using Microsoft Office Excel 2016 spreadsheet. For illustrations, averaged values for each measurement of both groups were calculated separately for occipital hemispheres and distractor types. Averaged values of 4800 ms epochs for both intervention groups and measurement times are illustrated in *Figure 3.*

Power waveforms revealed that alpha power modulated with respect to the task between visual distractor picture and retrieval picture appearances, regardless of distractor type and hemisphere being examined. First, the alpha power seems to decrease after the visual responses generated by the distractor picture for approximately 500 ms, and secondly it seems to increase for approximately 700 ms, prior to the visual responses generated by the retrieval picture appearance at 1500 ms. Thus, based on the information offered by averaged charts, two separate time windows were determined to examine the alpha power change. Alpha decrease time window was defined from 300 ms to 800 ms and alpha increase time window was defined from 800 ms to 1500 ms. The starting point for the alpha decrease window was defined to 300 ms to ensure that the visual responses of distractor picture would no longer cause interference, and the point between time windows was defined to 800 ms based on alpha power increase. The end point of the alpha increase time window was defined to 1500 ms to ensure that the visual responses caused by retrieval picture do not cause any interference.

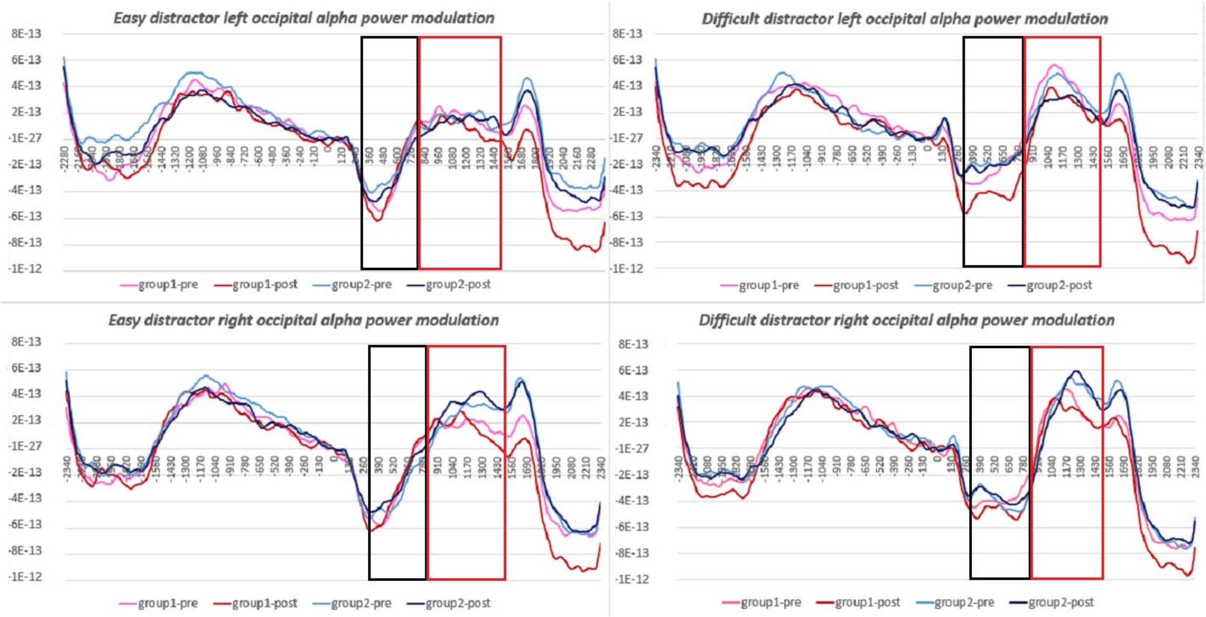

Figure 3. *Averaged power waveforms of both groups' pre- and post-intervention measurements divided by hemisphere and distractor type representing modulation of alpha power during the task. Group 1 stands for PTCT group and group 2 stands for PT group. The X-axis point zero indicates distractor appearance. Black rectangles indicate alpha decrease time window and red rectangles indicate alpha increase time window.*

Thus, eight comparable statistical variables of alpha power modulation were created for both groups in both time windows – left and right occipital alpha responses to easy distractor in a pre-intervention measurement, LPREASY and RPREASY, and left and right occipital alpha responses to difficult distractor in a pre-intervention measurement, LPRDIFF and RPRDIFF. Correspondingly, left and right occipital alpha responses to easy and difficult for post-intervention measurements were named LPOEASY, RPOEASY, LPODIFF and RPODIFF.

Statistical analysis

The effects of the 12-month-long combined physical and cognitive training program on occipital alpha-band power in two time windows were analyzed using repeated measures ANOVAs with hemisphere (left occipital and right occipital), measurement (pre and post), and distractor (easy and difficult) as within-subjects factors and group (PTCT and PT) as a between-subjects factor. In addition, the effect of visual distractor difficulty level on occipital alpha-band power was tested using paired samples t-tests (planned contrast) comparing responses of the same measurement and hemisphere between easy and difficult visual distractors in both time windows. When the repeated measures ANOVAS indicated any significant interaction effects, follow-up ANOVAs were conducted separately for significant interactions. The level of statistical significance was determined as p-value being .05 or less. Normality checks were carried out to the residuals which were approximately normally distributed. All statistical analyses were completed with IBM SPSS Statistics 24 software program.

Results

The following section presents the results of the 12-month-long combined physical and cognitive training program on occipital alpha-band power modulation during a visual working memory task. First, the results of the 'alpha decrease' time window (300-800ms after distractor appearance) are presented and second, the results of the 'alpha increase' time window (800-1500 ms after distractor appearance) are presented.

Training program effects in alpha decrease time window

Repeated measures ANOVA

Repeated measures ANOVA in 300-800 ms time window showed no significant main effect of group, F(1,22) = .269, p = .609, η_p^2 = .012. However, it indicated that there was a significant effect of hemisphere on alpha power, F(1,22) = 8.911, p = .007, η_p^2 = .288. Averaged alpha power was significantly lower in right occipital areas (M = -3.629, SE = .681) than it was in left occipital areas (M = -2.545, SE = .532). See *Figure 4.* There were no other significant interaction effects with hemisphere: hemisphere*group, F(1,22) = .908, p = .351, η_p^2 = .040, hemisphere*measurement, F(1,22) = 2.335, p = .141, η_p^2 = .096, hemisphere*measurement*group, F(1,22) = .222, p = .642, η_p^2 = .010, hemisphere*distractor, F(1,22) = 2.132, p = .158, η_p^2 = .088, hemisphere*distractor*group, F(1,22) = .803, p = .380, η_p^2 = .035, hemisphere*measurement*distractor, F(1,22) = .065, p = .801, η_p^2 = .003, or hemisphere*measurement*distractor*group, F(1,22) = 2.992, p = .098, η_p^2 = .120.

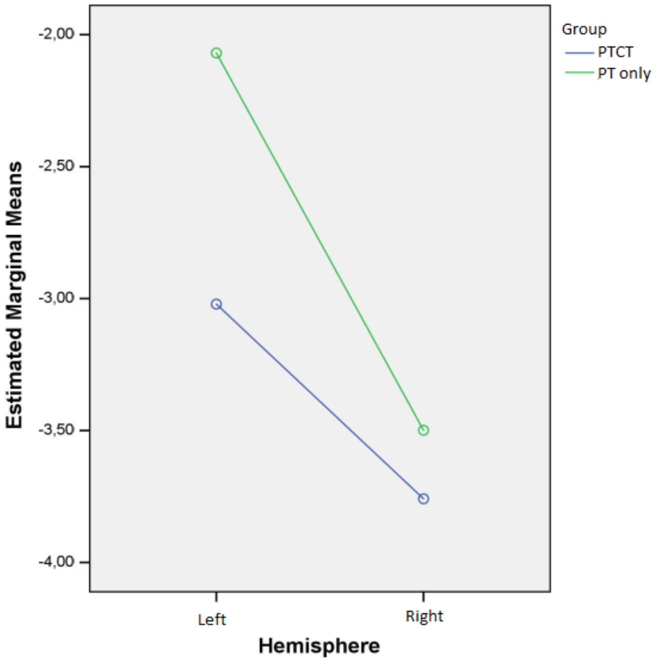

Figure 4. *Estimated marginal means of alpha power in both hemispheres.*

Measurement time showed neither a significant main effect, F(1,22) = .986, p = .332, η_p^2 = .043, nor significant interaction effects with group, F(1,22) = 1.086, p = .309, η_p^2 = .047, or distractor, F(1,22) = 2.269, p = .146, η_p^2 = .093. Neither measurement*distractor*group was significant, F(1,22) = 2.959, p = .099, η_p^2 = .119.

However, there was a significant main effect of distractor on alpha power, F(1,22) = 4.592, p = .043, η_p^2 = .173. Averaged alpha power was significantly lower in response to difficult visual distractors (M = -3.455, SE = .690) than it was in response to easy visual distractors (M = -2.719, SE = .513). See *Figure 5.* Distractor and group did not indicate an interaction effect, F(1,22) = 1.817, p = .191, η_p^2 = .076. Mean scores and standard deviations of categorized variables used in the first time window are presented in *Table 3.*

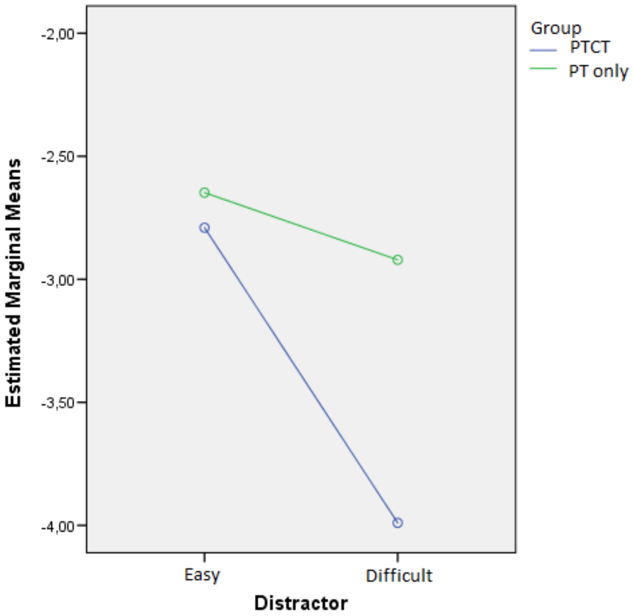

Figure 5. *Estimated marginal means of alpha power in response to easy and difficult distractors.*

Table 3. *Mean values and standard deviations of averaged alpha power categorized by group, occipital hemisphere, distractor difficulty and measurement time in the alpha decrease time window (300-800 ms).*

Hemisphere	**Group**	**Pre, M (SD)**		**Post, M (SD)**	
Distractor		***Easy***	***Difficult***	***Easy***	***Difficult***
Left occipital	**PTCT**	-2.52 (2.60)	-2.65 (4.17)	-2.39 (2.45)	-4.52 (4.60)
	PT	-1.75 (2.62)	-1.96 (2.42)	-2.43 (2.67)	-2.14 (2.51)
Right occipital	**PTCT**	-3.16 (3.06)	-3.96 (4.39)	-3.09 (3.21)	-4.83 (4.31)
	PT	-3.51 (3.29)	-3.95 (3.60)	-2.90 (2.45)	-3.64 (3.81)

Pre-planned contrasts of distractor difficulty in alpha decrease time window

For testing the secondary hypothesis in the first time window, four paired samples t-tests were conducted to make comparisons between easy and difficult distractor induced responses in alpha power within the same hemisphere and at the same time of measurement. There was no significant difference in alpha power between difficult and easy distractor in the left occipital alpha power in the pre-intervention measurement (easy M = -2.07, SD = 2.59, difficult M = -2.24, SD = 3.20; t(23) = .430, p = .671). Neither there was a significant difference in alpha power between difficult and easy distractor in the right occipital alpha power in the pre-intervention measurement (easy M = -3.37, SD = 3.14, difficult M = -3.96, SD = 3.85; t(23) = 1.313, p = .202).

Further, there was no significant difference in alpha power between difficult and easy distractor in the left occipital alpha power in the post-intervention measurement (easy M = -2.42, SD = 2.53, difficult M = -3.13, SD = 3.64; t(23) = 1,257, p = .221). However, there was a significant difference in alpha power between difficult and easy distractor in the right occipital alpha power in the post-intervention measurement (easy M = -2.98, SD = 2.73, difficult M = -4.13, SD = 3.98; t(23) = 2.925, p = .008).

Training program effects in alpha increase time window

Repeated measures ANOVA

Repeated measures ANOVA in 800-1500 ms time window showed no main effect of group, F(1,22) = .338, p = .567, η_p^2 = .015. Further, it showed no significant main effect of hemisphere on alpha power, F(1,22) = 1.411, p = .248, η_p^2 = .06. However, there were two significant interaction effects with hemisphere and measurement, F(1,22) = 4.755, p = .04, η_p^2 = .178, and hemisphere and distractor F(1,22) = 8.919, p = .007, η_p^2 = .288. In addition, main effect of distractor showed a trend of significance on alpha power, F(1,22) = 4.076, p = .056, η_p^2 = .156. Averaged alpha power was nearly significantly higher in response to difficult distractors (M = 2.414, SE = .555) than it was in response to easy distractors (M = 1.719, SE = .346)

To further examine the interactions between hemisphere*measurement and hemisphere*distractor, follow-up repeated measures ANOVAs were conducted separately for left occipital hemisphere and right occipital hemisphere. The left hemisphere follow-up repeated measures ANOVA showed a significant main effect of measurement time on alpha power, F(1,22) = 8.581, p = .008, η_p^2 = .281. Averaged alpha power in left hemisphere was significantly higher in the pre-intervention measurement (M = 2.302, SE = .423) than it was in the post-intervention measurement (M = 1.480, SE = .414). See *Figure 6.1.* Moreover, there was a significant main effect of distractor on alpha power, F(1,22) = 11.708, p = .002, η_p^2 = .347. Averaged alpha power in the left hemisphere was significantly higher in response to difficult distractors (M = 2.538, SE = .530) than it was in response to easy distractors (M = 1.244, SE = .318). See *Figure 6.2.* No significant interactions were found. The right hemisphere follow-up ANOVA showed neither significant main effects nor interactions.

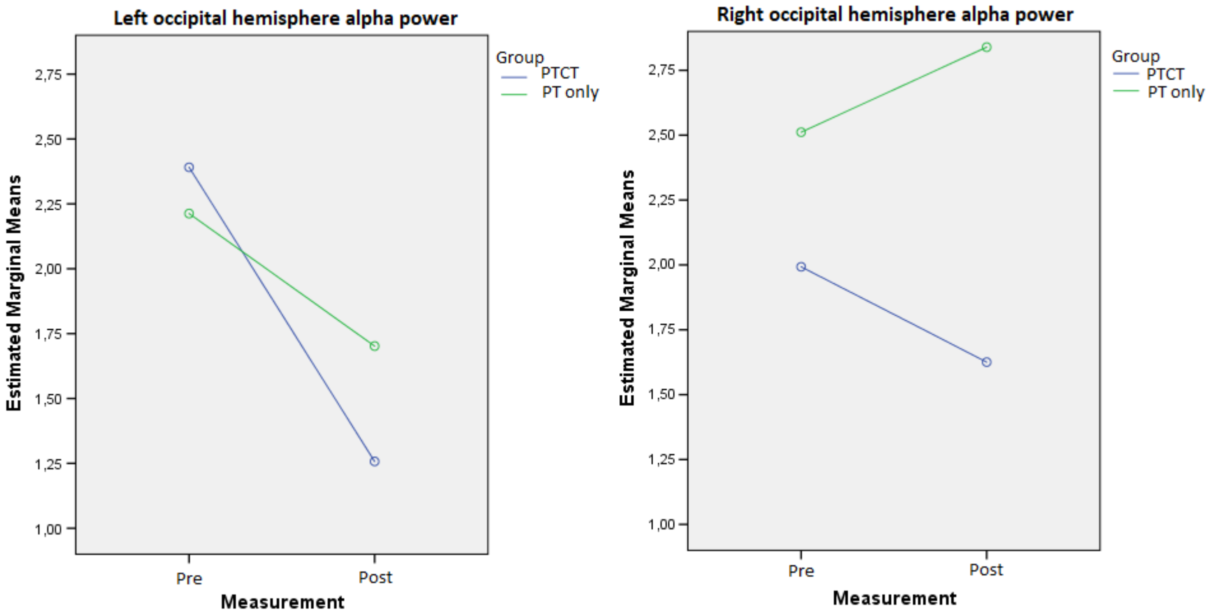

Figure 6.1. *Estimated marginal means of alpha power in left and right hemispheres during pre- and post-intervention measurements.*

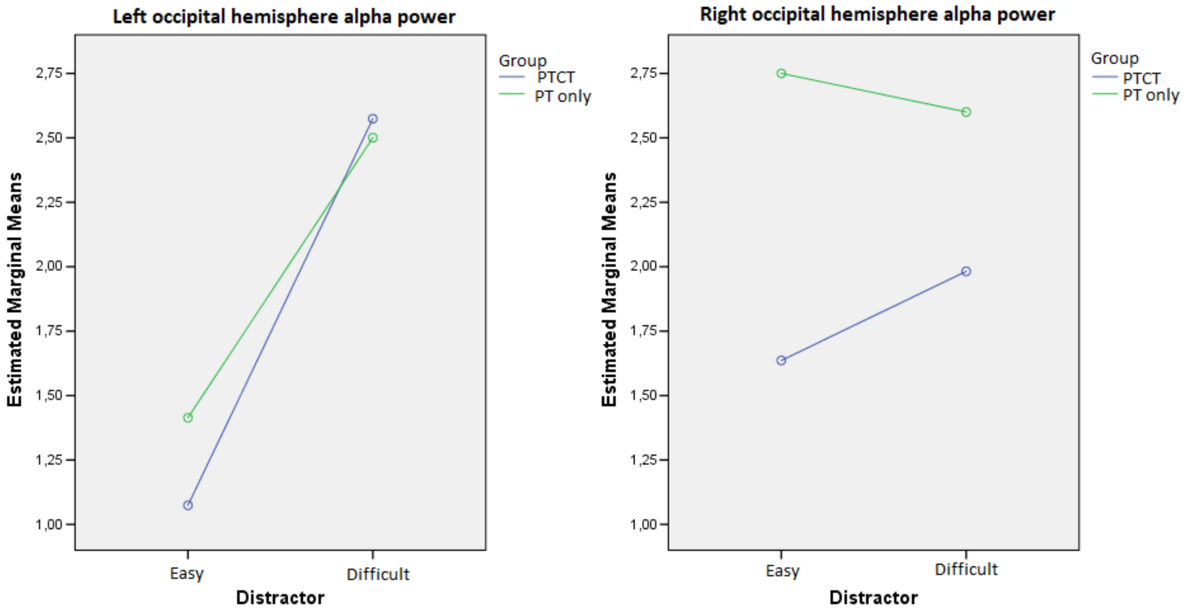

Figure 6.2. *Estimated marginal means of alpha power in left and right hemispheres in response to easy and difficult distractors.*

In the primary repeated measures ANOVA, hemisphere did not have any other significant interaction effects: hemisphere*group, F(1,22) = 1.534, p = .228 η_p^2 = .065, hemisphere*measurement*group, F(1,22) = .010, p = .923, $\eta_p^2 < .001$, hemisphere*distractor*group, F(1,22) = .011, p = .919, $\eta_p^2 < .001$, hemisphere*measurement*distractor, F(1,22) = .289, p = .596, η_p^2

= .013 or hemisphere*measurement*distractor*group, F(1,22) = .116, p = .737, η_p^2 = .005. Furthermore, measurement time showed neither a significant main effect, F(1,22) = 2.267, p = .146, η_p^2= .093, nor significant interaction effects with group, F(1,22) = 1.388, p = .251, η_p^2 = .059, or distractor, F(1,22) = 1.09, p = .308, η_p^2 = .047, and neither did measurement*distractor*group, F(1,22) = .010, p = .921, η_p^2 < .001. As well, distractor*group interaction showed no significant interaction effect, F(1,22) = .435, p = .516, η_p^2 = .019. Mean scores and standard deviations of categorized variables used in the second time window are presented in *Table 4.*

Table 4. *Mean values and standard deviations of averaged alpha power categorized by group, occipital hemisphere, distractor difficulty and measurement time in the alpha increase time window (800-1500 ms).*

Hemisphere	**Group**	**Pre, M (SD)**		**Post, M (SD)**	
Distractor		***Easy***	***Difficult***	***Easy***	***Difficult***
Left occipital	**PTCT**	1.46 (1.79)	3.32 (2.73)	0.69 (1.54)	1.82 (2.98)
	PT	1.50 (1.68)	2.93 (2.83)	1.33 (1.68)	2.08 (2.62)
Right occipital	**PTCT**	1.74 (1.68)	2.24 (3.80)	1.53 (1.92)	1.72 (3.47)
	PT	2.44 (1.93)	2.58 (2.84)	3.06 (2.96)	2.62 (3.83)

Pre-planned contrasts of distractor difficulty in alpha increase time window

For testing the secondary hypothesis in the second time window, four paired samples t-tests were conducted to make comparisons between easy and difficult distractor induced responses in alpha power within the same hemisphere and at the same time of measurement. There was a significant difference in alpha power between difficult and easy distractor in the left occipital alpha power in the pre-intervention measurement (easy M = 1.48, SD = 1.69, difficult M = 3,09, SD = 2.73; t(23) = -3.668, p = .001). However, there was no significant difference in alpha power between difficult and easy distractor in the right occipital alpha power in the pre-intervention measurement (easy M = 2,15, SD = 1.83, difficult M = 2.44, SD = 3.20; t(23) = -.569, p = .575).

Further, there was a significant difference in alpha power between difficult and easy distractor in the left occipital alpha power in the post-intervention measurement (easy M = 1.06, SD = 1.62, difficult M = 1.97, SD = 2.72; t(23) = -2.088, p = .048). However, there was no significant difference in alpha power between difficult and easy distractor in the right occipital alpha power in the post-intervention measurement (easy M = 2.43, SD = 2.64, difficult M = 2.24, SD = 3.63; t(23) = .335, p = .741).

Discussion

The purpose of this study was to examine the effects of 12-month physical and cognitive training program on brain basis of inhibitory control among the elderly people. No differences in occipital alpha power modulation between the groups were found in either of examined time windows. Based on data observation, occipital alpha-band modulation seemed to modulate in two time windows in the period between the distractor appearance and retrieval picture appearance. Immediately after the disappearance of distractor-induced visual responses in occipital areas, alpha-band power decreased considerably for approximately 500 milliseconds. In the subsequent time window, alpha-band power increased rapidly for about 500 milliseconds and remained, or mildly decreased until the appearance of visual responses generated by a retrieval picture. For this reason, it was decided to examine the alpha power modulation separately in two time windows. Although the graphical examination of distractor induced desynchronization in the first time window partly indicated group differences, none were found in this study. The alpha power variation subsequent to the distractor picture could be related to the two ongoing and overlapping cognitive processes of the subjects - meanwhile subjects need to actively suppress the visual information of a distractor they also need to strive to retain the facial characteristics of an encoding picture. By analyzing the results in two time windows, it would be possible to obtain more accurate information on the processing of hemispheres during the dual-task inhibition phase.

In addition to the primary hypotheses, other absorbing observations can be found on the results of analyses. In the first time window, alpha desynchronization was more intense in the right occipital hemisphere. Furthermore, alpha desynchronization was more intense in response to difficult distractors. The results of alpha-band power modulation in response to distractor difficulty supports the hypothesis of Zanto et al. (2010), according to which the stimuli containing complex information could be more challenging to suppress compared to simple-feature stimuli, especially among the elderly. In addition, recent and partly unexpected results of distractor inhibition study by Schroeder et al. (2018) gained support from the observed association between alpha power decrease and distractor difficulty. Noting that suppression of distractors was hypothesized to be in association with alpha synchronization, results could signal that alpha power decrease in the first time window could be at least partly involved in memory retaining of the encoding picture presented prior to a distractor.

Observed alpha power differences between the hemispheres may be related to the functions of facial recognition areas of the occipital hemispheres. According to previous observations, occipital face area (OFA) especially in the right hemisphere would be involved in detecting early stage facial features from visual stimuli (Pitcher, Walsh, Yovel & Duchaine, 2007). The observation coincides with the fact that occipital face recognition areas are ordinarily, though not always, located in the right hemisphere (Barton, Press, Keenan & O'Connor, 2002; Pitcher, Walsh & Duchaine, 2011*)*. Observed pattern of hemispheric differences is also supported by inspection of pre-planned contrasts, according to which, alpha desynchronization in the latter measurement was greater in response to difficult distractors than in response to easy distractors particularly in the right occipital areas. Together, the results of hemisphere differences in alpha power modulation could be interpreted as a certain kind of hemispheric and neuronal sensitivity for processing of facial characteristics.

Although no differences between the groups were found in the second time window, the results between two time windows examined seem to be fairly divergent. Examining observed interactions in the second time window, two follow-up ANOVAs conducted separately for each hemisphere indicated that both interactions are due to an alpha power modulation differences in the left occipital hemisphere. Taking a more detailed look on the alpha increase window results, left hemisphere alpha synchronization was more intense during the pre-intervention measurement, and in addition, left hemisphere alpha synchronization was more intense in response to difficult distractors. These findings further support the tentative thought of two different ongoing cognitive processes for about 1500 milliseconds after the appearing of a distractor picture - suppressing the irrelevant stimuli while simultaneously retaining information relevant to the task produces clearly perceptible oscillatory differences between the brain areas involved on the overlapping dual-task processing. However, left occipital alpha power decrease between the measurements raises questions and requires further investigation - it could originate from the training program's facilitative effects and be a marker of enhanced cognitive function. Though, further implications are impossible to be done without no-treatment control group. The dominance of the left hemisphere in the alpha increase time window is potentially an outcome of functional differences in the extrastriate face-sensitive visual regions (Puce, Allison, Gore & McCarthy, 1995). Furthermore, because the observed interactions in the second time window appeared to be a consequence of changes in left hemispheric activation, it is worth noting that the trend of difficult distractor-induced more intense alpha power changes seems to be supported also in the results of the latter time window. However, it is also possible that the processes of the first time window are more related to visual processing and the second time window may reflect more generalized memory processing, in which case the activation of the left hemisphere is involved only in the later stages of processing.

Again, observed pattern of hemispheric differences is also supported by inspection of pre-planned contrasts, according to which, alpha synchronization in the both times of measurement was greater in response to difficult distractors than it was in response to easy distractors particularly in the left occipital areas. The foregoing holds good even though the overall alpha-band power in the left occipital areas seemed to decrease between the pre- and post-intervention measurements. In conclusion of the results, during the alpha decrease phase the changes seem to center around right occipital areas while the alpha increase phase changes seem to focus in the regions of left occipital hemisphere. The result shows that cognitive reactions and the level of suppression in response to different distractor types evidently differ. In this respect, the secondary hypothesis of the study was supported.

Although the primary hypotheses of the study did not receive support from the results, the strengths and weaknesses of the study should be considered. Observing the effects of particular skill training on cognitive processes and their brain-level responses, special consideration should be given to the duration and intensity of skill training, and in addition, characteristics of the task (Brisswalter, Collardeau & René, 2002). As stated above, comparing the benefits of physical activity among the elderly, the effects seem to appear most beneficial on tasks that require processing of visuospatial information (Shay & Roth, 1992). The observation supports the selection of a visual working memory task as the method to be used in the study. Taking a look on the duration of the training program, preliminary data from the field suggests that preserving brain function and creating a protective effect against mild cognitive impairment and AD on the elderly would require approximately 12 months of regular mild-to-moderate physical training (Duzel, van Praag & Sendtner, 2016). Thus, the duration of training program seems to be sufficient to provide protection against aging-related neural degeneration.

However, Duzel et al. (2016) also hypothesize that instead of preserving cognitive functions, improving the functions could be possible with remarkably shorter intervention. Interventions lasting only from 3 to 6 months have provided indications of slightly improved cognitive functions on the elderly, demanding that the intensity and frequency of training sessions have been raised to a moderate-to-high level (Duzel et al., 2016). A program with shorter duration but increased intensity could be less demanding to commit until the end of the program. All subjects who discontinued the study were members of PTCT group - this raises a question of the incidence of the excessive stress among combined training program participants. By adjusting the overall duration, frequency and intensity of the training program and by remodeling the proportion between physical and cognitive training sessions, it is possible to construct a training program that is both more engaging and more effective. For instance, adherence to higher intensity and frequency training program is certainly possible if the overall duration of the program is kept shorter. These kinds of changes also aim to target at different mechanisms of brain-level effects.

Although no differences were found between the groups in this study, comparing protective factors with this experimental design is not entirely trouble-free. Taking a closer look at the limitations of the study, the subjects participating in the physical training program acted as the control group of the study while subjects in the experimental group participated in combined physical and cognitive training program. Thus, both groups of the study have received treatment that in the light of a prior knowledge could be expected to influence the measured variables. In other words, without the actual control group it is challenging to reflect whether the effect of time is due exercising protective factors - it is plausible that both groups are trained because they have both been practicing the protective factors, albeit in divergent proportions. In particular, the interpretation of the observed alpha decrease effect in left occipital hemisphere is somewhat challenging due to an experimental set-up.

In addition, this study focused solely on the specific brain-level mechanisms of the effects of the training program. Proposing new possibilities for future research, a comparative design between brain-level changes and cognitive assessment test scores would produce information that would enable applying of new findings to practical problems of the field. Furthermore, Zhu et al. (2017) have noted that the majority of published studies have used self-reported assessments as a measure of training, and the manner is causing biases especially among the elderly.

Applying objectively measured physical and cognitive training to upcoming experiments would provide faultless data for research applications. In conclusion, the foregoing proposals for future research offer an opportunity to approach the theme in a more diverse manner, but in line with the results of this study. By applying the duration, intensity and proportion of the sessions in the training program, by connecting the cognitive test assessments scores and objectively measuring the time spent on training in an experimental setting with control group receiving no treatment, the upcoming research will refine the findings of this study and provides additional information on functional differences between the hemispheres during working memory inhibition tasks. The ultimate objective for the future is to develop different training programs to meet the challenges of different patterns of aging, and the objective is achieved by revising and modifying the above-mentioned elements in individually designed proportions.

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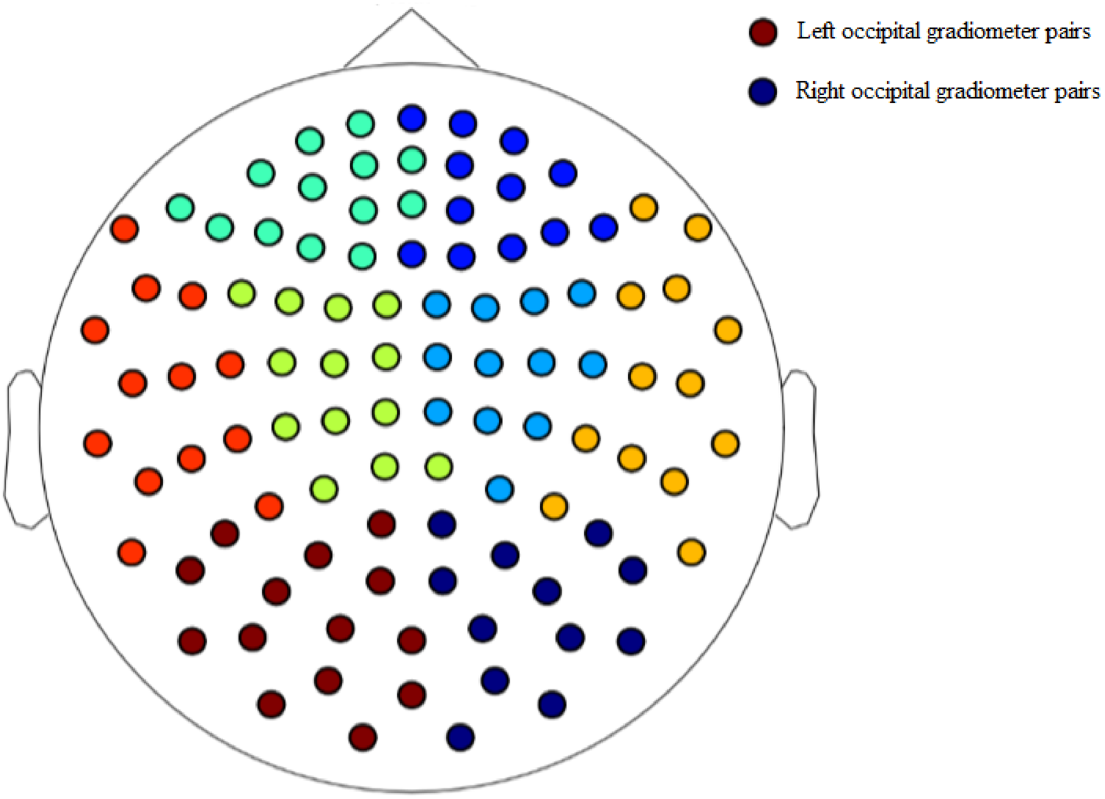
Appendix



Appendix 1. *Left occipital MEG gradiometer pairs used in the study are marked with dark red and right occipital gradiometer pairs used in the study are marked with dark blue.*

Effect (left hemisphere)	F	df, error df	p	η_p^2
Group	.029	1,22	.867	.001
Measurement	8.581	1,22	.008**	.281
Measurement*Group	1.231	1,22	.279	.053
Distractor	11.708	1,22	.002**	.347
Distractor*Group	.299	1,22	.590	.013
Measurement*Distractor	2.058	1,22	.165	.086
Measurement*Distractor*Group	.003	1,22	.960	.000

Effect (right hemisphere)	F	df, error df	p	η_p^2
Group	.729	1,22	.403	.032
Measurement	.003	1,22	.959	.000
Measurement*Group	.831	1,22	.372	.036
Distractor	.055	1,22	.817	.002
Distractor*Group	.352	1,22	.559	.016
Measurement*Distractor	.421	1,22	.523	.019
Measurement*Distractor*Group	.038	1,22	.847	.002

Appendix 2. *Results of two follow-up repeated measures ANOVAs of 'alpha increase' time window made separately for left and right occipital hemisphere. Symbols of statistical significance;*

$* p \leq .05$; $** p \leq .01$; $*** p \leq .001$.