THE EFFECTS OF COMBINED COGNITIVE AND PHYSICAL INTERVENTION ON INHIBITORY FUNCTIONS AND THE MODULATION OF ALPHA OSCILLATIONS DURING INHIBITION TASKS

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ABSTRACT

Ageing is known to cause changes in the structure, metabolism, and oscillatory functions of the brain. These changes in the brain cause non-pathological cognitive decline in various cognitive functions, such as executive functions, processing speed, and memory.

One of the cognitive functions affected by ageing is inhibition. Changes in inhibitory functions are reflected in brain oscillations, which are spontaneously arising changes of the rhythmicity in local field potentials. Inhibitory functions have been found to be associated with greater power of alpha oscillations (8-13 Hz) during distracting stimuli. This thesis aims to examine whether a 12-month combined physical and cognitive training intervention (PTCT) effects the inhibitory functions of older adults more than a physical training intervention (PT) alone. The effects of a combined intervention are studied by using both cognitive tests and measurements of electrical functioning in the brain. The changes in temporal modulation of alpha power due to inhibition tasks are compared between a baseline measurement and a 12-month assessment in the frontal and occipital regions of the left and right hemisphere in both the physical training and the combined physical and cognitive training groups. Differences in inhibitory functions between the two measurements and groups are also examined by comparing the total number of errors made in both Stroop test and Trail Making Test A and B.

Twenty-four community-dwelling sedentary men and women (men n=8, women n=16) born between 1935 and 1946 took part in the study. Participants were randomized into two training programs: the physical training program (PT) and the physical and cognitive training program (PTCT). First a baseline measurement of alpha oscillations and cognitive functions was established, followed by a 6-month and 12-month evaluation. The baseline measurement and 12-month evaluation were selected for further analysis. Alpha oscillations were recorded using magnetoencephalography (MEG). During the MEG recording participants answered to a visual working memory task, including three pictures of which the second picture was an easy or difficult distractor. Participants then had to decide whether the first and the third picture shown were the same, trying to inhibit the distraction picture.

There were no significant differences in mean alpha modulation between the measurement times or between the intervention groups. General alpha power was found to be significantly stronger in the occipital area compared to the frontal area. No significant differences between the measurements and the intervention groups were found in Stroop test or Trail Making Test. In conclusion, physical intervention or combined cognitive and physical intervention did not improve inhibitory functions. Furthermore, no changes in alpha oscillations related to inhibitory functions were observed. These results might be due to a relatively small sample size, lack of effectiveness of the intervention program, and good cognitive skills of the participants. For future research it would be essential to study the role of different intervention types and the importance of alpha oscillations as well as other oscillations in inhibitory functions.

Keywords: inhibition, ageing, physical intervention, cognitive intervention, MEG, alpha oscillations

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Ikääntymisen tiedetään aiheuttavan muutoksia aivojen rakenteessa, metaboliassa ja oskillaatioissa. Nämä muutokset saavat aikaan ei-patologista kognitiivista heikkenemistä muun muassa eksekutiivisissa toiminnoissa, prosessointinopeudessa ja muistissa.

Yksi kognition osa-alue, johon ikääntymisen on todettu vaikuttavan, on inhibitio. Muutokset inhibitorisissa toiminnoissa heijastuvat oskillaatioissa, spontaanisti syntyvissä paikallisten kenttäpotentiaalien rytmisyyden muutoksissa. Inhibition on todettu olevan yhteydessä suurempaan alfa-rytmin (8-13 Hz) voimakkuuteen häiritsevän ärsykkeen ollessa läsnä ja tämä voimakkuuden kasvu ilmenee niillä aivoalueilla, joita käytetään aktiivisesti osana tiedonkäsittelyä. Tämän pro gradu -tutkielman tarkoituksena on selvittää, vaikuttaako 12 kuukauden mittainen yhdistetty liikunta- ja kognitiivinen interventio (PTCT) ikääntyvien inhibitorisiin toimintoihin enemmän, kuin pelkkä liikuntainterventio (PT). Yhdistetyn intervention vaikutuksia tarkastellaan sekä kognitiivisilla testeillä, että aivojen sähköisen toiminnan mittauksilla. Alfa-oskillaatioiden voimakkuuden muutoksia verrataan alkumittauksen ja 12 kuukauden loppumittauksen välillä, vasemman ja oikean aivopuoliskon välillä ja otsalohkon ja takaraivolohkon välillä, sekä yhdistetyn intervention ja liikuntaintervention välillä. Eroja inhibitiossa mittausajankohtien ja interventioryhmien välillä tutkitaan myös vertaamalla kokonaisvirheiden määrää Stroop -testissä ja Trail Making Test -testissä.

24 tervettä, vähän liikkuvaa, vuonna 1935 - 1946 syntynyttä, miestä ja naista (miehet n=8, naiset n=16) osallistui interventioon. Koehenkilöt satunnaistettiin kahteen ryhmään: liikuntaharjoitteluryhmään (PT) ja liikunnan ja kognitiivisen harjoittelun ryhmään (PTCT). Alfa-oskillaatioiden mittaukset ja kognitiiviset testit tehtiin ennen intervention alkamista, kuuden kuukauden päästä ja 12 kuukauden päästä aloittamisesta. Tilastollisilla testeillä verrattiin alkumittauksen ja loppumittauksen tuloksia. Alfa-oskillaatioita mitattiin käyttämällä magnetoenkefalografiaa (MEG). MEG -mittausten aikana koehenkilöt vastasivat visuaaliseen työmuistitehtävään, joka sisälsi kolme kuvaa, ja joista toinen oli helppo tai vaikea häiriökuva. Koehenkilöiden tehtävänä oli vastata, olivatko ensimmäinen ja viimeinen esitetty kuva sama, yrittäen inhiboida häiriökuvan.

Alku- ja loppumittausten ja interventioryhmien välillä ei löydetty tilastollisesti merkitseviä eroja, mutta yleinen alfa-oskillaatioiden voimakkuus oli merkitsevästi suurempia takaraivolohkossa verrattuna otsalohkoon, mikä vastasi odotuksiamme. Eroja mittausajankohtien ja ryhmien välillä ei löydetty Stroop -testissä tai Trail Making Test -testissä. Tulosten perusteella voidaankin todeta, ettei liikuntainterventiolla tai yhdistetyllä liikunta- ja kognitiivisella interventiolla ole vaikutusta alfa-aktivaation tehoon tai inhibitioon. Tulosten voidaan mahdollisesti katsoa selittyvän myös pienellä otoskoolla, intervention mahdollisella tehottomuudella tai koehenkilöiden hyvillä kognitiivisilla kyvyillä. Tulevien tutkimusten olisi tärkeää perehtyä tarkemmin käytetyn intervention rooliin, sekä alfa-oskillaatioiden ja muiden oskillaatioiden rooliin inhibitorisissa toiminnoissa.

Avainsanat: inhibitio, ikääntyminen, liikuntainterventio, kognitiivinen interventio, MEG, alfa-oskillaatiot

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1. INTRODUCTION

1.1 The Ageing Brain and Cognition

As a result of developments in healthcare and improved standards of living in many societies, the average life expectancy is increasing, hence there are more and more elderly people among the population (Bloom et al., 2011). Because the brain and cognitive abilities are known to be affected by ageing, cognitive impairments are becoming more prevalent since more people are reaching older age (Suthers, Kim & Crimmins, 2003). As the risk of cognitive impairments increases exponentially as people age, the older the age group the higher the prevalence of cognitive impairments (Suthers, Kim & Crimmins, 2003). This non-pathological cognitive decrease is a normal consequence of ageing and may already start to appear in early adulthood, though especially in late adulthood (Salthouse, 2009). Cognitive decline has several malign influences on well-being and experienced quality of life of an individual since it usually restricts the ability to live independently (Deary et al., 2009). Furthermore, moderate or severe cognitive impairment has been correlated with increased risk of death (Langa et al., 2008). Additionally, treatment of cognitive impairment is costly for society (Deary et al., 2009).

Consequently, ageing-related cognitive decline causes significant disadvantages for both individuals and society at large, and therefore actions to minimize ageing-related cognitive decline among the population are crucial. However, to prevent this ageing-related cognitive decline it is important to understand the factors behind this phenomenon.

There are several biological factors to explain ageing-related cognitive decline. One of the reasons is cerebral atrophy; a decrease in the size and density of the brain in which both white and grey matter are affected, especially in the frontal and temporal lobes (Murman, 2015). A decrease in white matter integrity causes a decrease in information processing speed, since white matter is related to transporting information between different areas of the brain (Deary et al., 2009). More specifically, both axons and myelin show degeneration with age (Madden et al., 2012). Myelin is a substance that covers axons and it has a significant role in increasing axonal conduction velocity, therefore disturbances in myelination have been linked to cognitive impairments such as impaired cognitive processing speed (Lu et al., 2013; Melie-Garcia et al., 2017). Ageing-related changes in white matter volume can also be detected in the frontal regions of the brain, and this white matter hyperintensity has also been associated with cognitive decline (Gunning-Dixon & Raz, 2003).

A decrease in grey matter volume seems to be of most significance in the prefrontal areas (Peters, 2006). Additionally, brain volume in the subcortical areas such as the striatum and the hippocampus are showing reductions in ageing, and for example hippocampal grey matter decrease has been linked with cognitive decline among elderly adults (Peters, 2006; Zanchi et al., 2017). Furthermore, Salat et al. (2004) discovered that this cortical thinning also expands to other brain areas, for example to the occipital areas, and it already begins to appear by middle age. According to Murman (2015), these changes in brain volume may be due to changes in synaptic structures, for example; synaptic loss, decrease in the number of axons and dendrites, and demyelination are all linked to normal ageing processes and affect cognitive performance.

All these biological changes highlight the major impact of ageing on the human brain, and since these biological changes are linked to cognition, ageing comes with significant changes in cognitive abilities. The effects of non-pathological cognitive decline are quite general and decline in one function may affect the others (Deary et al., 2009). For example, both selective and divided attention, retrieval and encoding of a memory trace, and mental flexibility are known to decline as a result of ageing (Murman, 2015). Particularly fluid cognitive abilities, which for example include executive functions, processing speed and memory, tend to show decrease already in middle age. Decrease of these functions, especially processing speed, affects negatively to other cognitive abilities (Deary et al., 2009). Furthermore, it has been shown that ageing reduces the capacity of working memory which works as a mediator between age and other cognitive abilities, such as episodic memory, spatial ability, and reasoning. (Verhaeghen et al., 2003) According to Deary et al. (2009), these fluid functions are especially significant for an individual’s independence and coping in every-day life, and therefore knowledge of these impairments is necessary to prevent them.

One of the key cognitive functions that undergoes ageing-related changes is inhibitory processes. Inhibitory processes refer to an ability to ignore task-irrelevant stimuli and to focus on stimuli relevant for the task (Borghini et al. 2018). Borghini et al. (2018) have discovered that ageing causes a decline in inhibitory processes. Changes in inhibitory processes significantly affect the performance of other cognitive abilities, for example working memory, and therefore inhibitory processes play a crucial role in human cognition (Borghini et al., 2018). Interestingly, changes in inhibitory functions may reflect moderate or even severe cognitive decline (Bélanger & Belleville, 2009). Bélanger and Belleville (2009) discovered that compared to healthy participants, participants with mild cognitive impairment or Alzheimer’s disease showed decreased inhibitory processes, i.e. a higher number of errors during inhibitory tasks. This may mean that decreased inhibitory processes reflect more severe cognitive impairments.

As inhibitory processes are crucial for performing certain cognitive tasks correctly, and therefore they are needed for coping in every-day life, inhibitory processes can be used as a good indicator for cognitive capacity to study ageing-related cognitive decline. Since they interact strongly with other cognitive processes, such as executive functions and working memory, inhibitory processes provide information about general cognitive development related to ageing (Borghini et al., 2018; Garavan et al., 2002). To study these ageing-related changes in inhibition and working memory in more detail, the best indicator is the oscillatory functions of the brain, as they are known to have an important role in the origins of inhibitory processes and working memory (Borghini et al., 2018). Problems in performing a task which includes inhibitory functions and working memory may reflect changes in brain function, with these changes manifesting themselves in brain oscillations (Borghini et al., 2018).

Brain oscillations are spontaneously arising changes in the rhythmicity of local field potentials and they demonstrate the excitability of local neuronal populations (Thut, Miniussi & Gross, 2012). Oscillations are therefore electrical activity caused by a population of neurons firing together (Klimesch, Sauseng & Hanslmayr, 2007). Inhibitory cells generate rhythmic changes which fluctuate between maximal inhibition and minimal inhibition (Klimesch, Sauseng & Hanslmayr, 2007). Oscillations range by their frequencies and different oscillations reflect different functional states of the brain (Linkenkaer-Hansen et al., 2001).

In particular, neural oscillations in the range of 8-13 Hz, called alpha oscillations, are related to many cognitive processes. For example, modulation of oscillations in the alpha band have been noted to be occurring during both working memory (Basar, Basar-Erogluc, Karakas & Schurmann, 2001; Jensen et al., 2002) and long-term memory tasks (Basar et al., 2001). Perhaps most importantly, alpha oscillations work as an attentional buffer which helps us to focus on relevant information and filter out distracting stimuli, and therefore alpha oscillations are needed to inhibit non task-relevant cortical areas (Cooper et al., 2003; Klimesch, 2012). Cooper et al. (2003) noted that internally directed attention and mental imagery was associated with greater mean alpha amplitudes than externally directed attention. They also discovered that when the task demands increased, so did the alpha amplitudes. These inhibitory processes have been identified as creating alpha activity in the prefrontal cortex (Klimesch, Sauseng & Hanslmayr, 2007). According to Bonnefond & Jensen (2012), when the brain is processing irrelevant information, i.e. distracting stimuli, alpha activity increases in the occipital areas and extends to the temporal areas as well.

More specifically, the role of alpha activity varies with the power of its amplitude, which is associated with changes in the synchronization of neurons (Klimesch, Sauseng & Hanslmayr, 2007).

Synchronization occurs when a local neuronal population is firing in synchrony, whereas desynchronization refers to a state in which the oscillatory activity of a large population of neurons is no longer firing synchronously (Klimesch, Sauseng & Hanslmayr, 2007). Event-related synchronization (ERS) which is associated with an increase in alpha power is related to inhibition processes (Klimesch, Sauseng & Hanslmayr, 2007). It can be detected for example during a task in which the participant has to ignore task-irrelevant stimuli. Conversely, event-related desynchronization (ERD) of alpha amplitudes, i.e. a decrease in alpha power, reflects the active processing of information and it appears when the participant is actively responding to a task-relevant stimulus (Klimesch, Sauseng & Hanslmayr, 2007). Furthermore, those areas of the brain which are not relevant for performing a given task show larger ERS and smaller ERD when compared to the task-relevant brain areas (Klimesch, Sauseng & Hanslmayr, 2007). This means ERD appears in those brain areas which are needed to perform the given task, whereas surrounding task-irrelevant areas show ERS, which refers to inhibitory processes (Klimesch, Sauseng & Hanslmayr, 2007). These changes in alpha power are known as alpha modulation, which provides important information about different functional states in human cognition (Janssens et al., 2018).

This evidence illustrates how alpha oscillations are crucial for several cognitive processes, and therefore we can assume that ageing-related cognitive decline is reflected in the changes of rhythmic activity in the brain. Related to this assumption, Volf and Gluhih (2010) studied ageing-related oscillatory changes by comparing groups of older participants to younger participants, discovering an age-related decrease in the total power of rhythmic activity at alpha range among the older age group. Furthermore, Borghini et al. (2018) studied this role of alpha oscillations in functional inhibitory processes and how it is affected by ageing. They found that inhibitory processes were reduced among elderly participants in comparison to younger participants, and that these changes were linked to a decrease in alpha power.

Altogether, ageing influences the brain in several ways and cognitive functions are affected by these ageing-related changes. However, even though many of these changes are the natural consequences of ageing, they are not necessarily permanent and their consequences may be reduced (Borghini et al., 2018). Ageing-related cognitive decline may be delayed with a physically and cognitively active lifestyle. It is widely known that individuals who use their cognitive capacity in every-day life are less vulnerable to cognitive impairment in later life (Deary et al., 2009). Moreover, research shows that physically active individuals remain in a more cognitively capable condition than individuals with a less physically active lifestyle (Deary et al., 2009). This evidence highlights the role of a physically and cognitively active lifestyle in preventing ageing-related cognitive decline.

Next we will introduce literature on studies depicting how physical exercise affects the brain and cognition in more detail.

1.2 The Effects of Physical and Cognitive Activity on the Brain and Cognition

Physical exercise has been proven to affect the brain and cognition via improving those structural and metabolic factors that are crucial for optimal cognitive performance. For example, aerobic exercise has been shown to increase brain volume in both grey and white matter in older adults (Colcombe et al., 2006). Aerobic exercise has also been found to change the volume of grey matter, especially in the frontal lobes and the areas of the cortex involved in attentional control and memory (Colcombe et al., 2006). Moreover, it has been discovered that a higher level of physical fitness is related to an increased volume of grey matter in the prefrontal and temporal areas of the brain, and an increased volume of white matter in the anterior areas, and that these effects are related to increased cognitive performance among older adults (Hillman, Erickson & Kramer, 2008;Colcombe et al., 2006).

Along with structural changes, there is evidence that physical exercise may also cause many changes in the functions of the brain. Studies using functional magnetic resonance imaging (fMRI) have shown adults high in cardiovascular fitness and participants in an aerobic fitness intervention group to show higher activation compared to inactive control groups in brain areas associated with effectual attentional control (Colcombe et al., 2004). Physical exercise also increases blood flow in the brain and this enhanced circulation has a positive effect on cognitive functions (Ainslie et al., 2008; Churchill et al., 2002; Maass et al., 2015). According to these findings, physical exercise has an important role to play in preventing ageing-related cognitive decline via improving neural circulation.

The effects of physical exercise are known to develop both several cognitive processes in general and more specifically by enhancing certain cognitive functions, particularly executive functions (Hillman, Erickson & Kramer, 2008). Inhibitory functions specifically are an essential factor of executive functions since inhibitory processes enable behavioural control and the ignoring of task-irrelevant stimuli (Garavan et al., 2002). The areas of the brain associated with executive functions are especially sensitive to ageing, and therefore physical exercise may be a preventive factor in delaying this ageing-related process (Hillman, Erickson & Kramer, 2008).

As illustrated in the above-mentioned studies, physical exercise is widely known to improve cognitive functions via affecting the structural and metabolic capacity of the brain.

Furthermore, it appears that the more diverse the intervention is, the stronger the effect on cognitive abilities, and therefore combining physical intervention with cognitive intervention might improve cognitive abilities more than physical intervention alone. In comparison to single cognitive or physical training, studies have shown simultaneous and subsequent cognitive and physical training to be more effective in improving cognitive skills such as attention, executive functions and working memory (Lauenroth, Ioannidis & Teichmann, 2016). Furthermore, combined physical and cognitive training may be used to improve performance in inhibitory tasks (Forte et al., 2013).

Additionally, combining aerobic exercise with strength training may improve cognition even further. Colcombe and Kramer (2003) determined that training interventions with older adults caused greater improvements in cognitive function with combined aerobic and strength training, compared to aerobic training alone, with improved fitness being most beneficial in enhancing executive control processes.

In conclusion, physical exercise has proven to be an efficient way to prevent, and also to treat, the non-pathological ageing-related decline of cognitive abilities. Physical exercise impacts the brain by enhancing its metabolic factors, resulting in an improved capacity for cognitive functions and an improvement in several cognitive skills (Ainslie et al., 2008; Churchill et al., 2002; Maass et al., 2015). However, there are still inconsistencies regarding which type of intervention is the most beneficial for cognitive improvement to occur. Some studies emphasize the role of combined cognitive and physical intervention (Lauenroth, Ioannidis & Teichmann, 2016), whereas other studies claim that cognitive improvement may be attained solely through physical or cognitive interventions (Forte et al., 2013).

Also the effects of physical and cognitive training on alpha reactivity during inhibition and memory tasks remains yet unsure. There is some research investigating the effects of physical exercise on alpha peak frequency, but only few studies have focused on alpha modulation (Gutmann et al., 2014). Since alpha modulation provides information of task-relevant and task-irrelevant responses, more research on the effects of physical exercise on alpha modulation during inhibition and working memory processes is needed.

1.3 Aim of the Study

The aim of this thesis is to study the effects of both a one-year physical intervention and a combined physical and cognitive intervention on the inhibitory functions of older adults during visual working memory tasks and through performance in cognitive tests. An increase in alpha power when presented with distracting stimuli during a working memory task is assumed to reflect improved inhibition, since alpha oscillations have been found to be related to inhibitory processes (Cooper et al., 2003; Klimesch, Sauseng & Hanslmayr, 2007; Klimesch 2012).

To study these changes in alpha power, magnetoencephalography (MEG) imaging will be used due to its high temporal resolution. In comparison with electroencephalography (EEG), MEG imaging can locate sites of activation with much higher accuracy. MEG allows us to directly observe brain activation during cognitive tasks. (Hari & Salmelin, 2012). Compared to other neuroimaging techniques measuring electrophysiological activity, such as EEG, MEG is less disrupted by layers of scalp, skull, and other head tissues, thus providing less biased data (Baillet, 2017). Therefore, MEG data is usually more precise than EEG data measured from the same source.

Several studies have shown combined physical and cognitive training interventions to be more effective in enhancing performance in tasks demanding inhibitory processes (Colcombe & Kramer, 2003; Forte et al., 2013; Lauenroth, Ioannidis & Teichmann, 2016). Therefore, it is assumed that combined physical and cognitive intervention will be more effective in improving inhibition during working memory tasks and increasing performance in cognitive tests, compared to physical training alone. However, earlier studies have focused on measuring improvements in inhibitory and working memory functions through performance in cognitive tests; but the effects of combined physical and cognitive intervention on the neural processes of inhibitory and working memory functions remain unclear.

Since alpha oscillations are known to relate to both inhibitory and working memory functions, it is crucial to study the effects of a combined physical and cognitive intervention on both cognitive performance and alpha oscillations. The power of alpha oscillations during inhibition of irrelevant information is compared between physical training intervention group and combined physical and cognitive intervention group. Analysis of alpha modulation in frontal and occipital areas will be assessed at the baseline measurement and the 12-month follow-up evaluation, to examine if the effects vary between different locations and measurement times. Cognitive test scores are compared between the two training groups at the baseline and 12 months after the baseline. Since this study will focus on how inhibitory processes are influenced by physical and cognitive interventions, performance in cognitive tests will be evaluated by the number of errors made in both Stroop test and Trail Making Test. Both tests are widely used to evaluate various cognitive functions, such as inhibition, processing speed, and mental flexibility, and are known to be sensitive to ageing (Comalli, Wapner & Werner, 1962; Houx, Jolles, Vreeling, 1993; Tombaugh, 2004). The frontal and occipital areas of the brain have been selected for analysis since both areas are known to be related to inhibitory processes. This study aims to investigate whether the inhibitory functions and cognitive skills of older adults may be improved with physical and cognitive interventions, possibly preventing cognitive impairment.

1.4 Hypothesis

Firstly, a combined intervention will affect alpha oscillations more than a physical intervention alone, and the power of alpha oscillations during distracting stimuli will be stronger after the intervention than compared to the original baseline measurement. Secondly, in comparison with the physical intervention alone, the combined intervention will improve performance in cognitive tests to a greater extent, and this effect will be seen as a reduced number of errors in Stroop test and Trail Making Test B.

2. METHODS

2.1 The PASSWORD Project

This thesis is part of the Brain sub-study of the PASSWORD Project (Physical and cognitive training intervention among older community-dwelling sedentary men and women), which was conducted in cooperation with the University of Jyväskylä's Department of Health Sciences and the Center for Interdisciplinary Brain Research (CIBR). The Brain sub-study aims to investigate the effects of a 12-month structured physical training program (PT), and a physical and cognitive training program, using magnetoencephalography (MEG) to record the results. The PASSWORD Project focuses on the effects of intervention on number of falls and on dual-task cost in walking speed.

2.2 Participants

The participants of the study were 24 community-dwelling sedentary men and women (men n=8, women n=16) born between 1935 and 1946. These participants were recruited to the PASSWORD Project from the population register of Jyväskylä. A letter containing information on the study was sent to a randomly selected group of 8000 70 – 85 year old inhabitants (⅔ of the 70 – 85 year old inhabitants of Jyväskylä). The inclusion criteria were: 1) in the age-range of 70 – 85, 2) living independently in Jyväskylä, 3) sedentary or moderately physically active lifestyle (less than 150 minutes of walking per week and no taking part in gym activities), 4) able to walk 500 meters, 5) a Mini Mental State Examination (MMSE) score of at least 24, 6) consent to participate. The exclusion criteria were: 1) serious chronic illness or medication affecting cognitive or physical functions, 2) immoderate and regular use of alcohol (more than 21 portion per week for men and 14 for women), 3) inability to participate in physical exercise or walking tests.

The participants were randomized into two separate training programs: the physical training program (PT), and the physical and cognitive training program (PTCT). All voluntary participants (n = 28) from both training programs were recruited to the MEG study. In total, 24 (women n=17, men n=7) participants took part in all three measurements of the MEG study. Fourteen participants took part in the physical training program and 10 participants in the physical and cognitive training program. Physical, cognitive and MEG assessments were done at the baseline and at six and 12 months after the baseline. Assessments done at the baseline and 12 months after the baseline were selected for further analysis.

2.3 Procedure

2.3.1 Physical Intervention

The interventions lasted for 12 months and included supervised weekly training sessions and independent home exercises. The supervised training sessions and home exercises were progressive; meaning the intensity, resistance, difficulty, and number of training sessions were all increased during the 12-month period. The home exercises aimed to support the adoption of an active lifestyle and the participants were advised to keep a diary of all independent exercises. Validated questionnaires and accelerometers (Gulf Coast Data Concepts, LLC, USA) were used to assess the level of physical activity.

The physical training group (PT) and the combined physical and cognitive training group (PTCT) both took part in multicomponent physical training; which included walking, resistance training, and balance training. Participants took part in one walking session per week, and one or two resistance and balance training sessions depending on the month. Home exercises included a progressive training program in gymnastics; with strengthening exercises, stretching, and balance training. Participants were encouraged to have around 150 minutes of moderate aerobic exercise per week. Walking, Nordic walking, cycling, and cross-country skiing were recommended exercises.

2.3.2 Cognitive Intervention

The combined physical and cognitive training group (PTCT) participated in cognitive training, which included computer-based training targeting working memory and executive functions. The cognitive training program was in-house developed (iPASS) and modified from the FINGER study (Finnish

Geriatric Intervention Study to Prevent Cognitive Impairment and Disability) (Ngandu et al., 2015). The cognitive training sessions were supervised and organized at the University of Jyväskylä. At the beginning of the training program, a supervised group session was organized to offer the participants support with their computer skills. Further support with their computer skills was also offered by the local University of the Third Age (UTA), and those whom did not have access to a computer for the home exercises, had the opportunity to complete them in ten different locations provided by the City of Jyväskylä (e.g libraries), where UTA-tutors would be present at certain times. The goal frequency for cognitive training was three to four times a week, lasting around 20 minutes each time. Each session consisted of four exercises organized into two blocks, which alternated between sessions. Block 1 included letter updating, spatial working memory maintenance, predictable set-sifting, and Stroop color tasks. Block 2 included spatial updating, spatial working memory maintenance, unpredictable set-sifting, and Stroop number tasks.

2.3.3 Physical Assessment

Physical measures included tests in walking, muscle strength, power, balance, body composition (DXA), and documenting the number of falls. Assessments were made of overall health, and safe participation was ensured by evaluating contraindications (ACSM guidelines) (Haskell et al., 2007) and acute conditions (blood count, CRP, Hb).

2.3.4 Assessment of Cognitive Performance

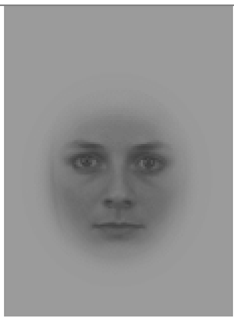
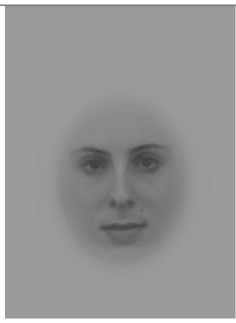
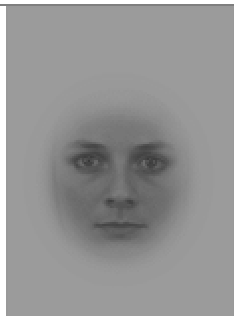
Cognitive performance was measured by using a test of global cognitive function (Consortium to Establish Registry for Alzheimer's Disease, CERAD total score) (Paajanen et. al., 2010) and a verbal fluency test (Letter Verbal Fluency Test) (Koivisto et. al., 1992). Executive functions were assessed with Stroop test (Graf, Uttl & Tuokko, 1995) and Trail Making Test A and B (Tombaugh, 2004). Stroop test consists of three sections; firstly, participants are instructed to read out a list of 72 words printed in black ink. Secondly, they are asked to name the color of 72 printed letter 'X' images. In the third section, the participants are shown 72 'color' words with incongruently colored inks (e.g. 'BLUE' is printed in red). Participants are instructed to name the color of the ink as fast as possible and ignore the word. Trail Making Test A and B are used to evaluate set sifting. In Trail Making Test A, participants are instructed to draw a continuous line connecting the numbers 1 through 25 in sequence. Trail Making Test B contains both words and letters, and participants are instructed to connect numbers and letters sequentially (e.g. number 1 to letter A, letter A to number 2) and continue until they reach the letter I. Participants are advised to perform the task as accurately and as quickly as possible.

2.3.5 MEG Measurements

In the present study, MEG measurements were used to study the effects of the PT and PTCT interventions on changes in alpha power. Magnetoencephalography or MEG is a neuroimaging technique used to measure electromagnetic fields of the brain (Hari & Salmelin, 2012). The source of the MEG signals are the pyramidal neurons of the cortex and their synchronous postsynaptic intracellular currents. Excitatory and inhibitory potentials flow through dendrites generating a dipolar current, which in turn creates the magnetic field of the brain when large group of neurons are simultaneously active (Proudfoot, 2014).

MEG measurements were conducted at the baseline and 6 and 12 months after the baseline. Data was collected with the Elekta Neuromag® system (Elekta Oy, Helsinki, Finland) with 306 channels and 102 sensor units, each containing one magnetometer and two gradiometers. The assessments consisted of a cognitive task in which participants first saw a picture of a human face, followed by distracting stimuli, which was either an easy distractor or a hard distractor. A grey oval shape without a face was used as an easy distractor, and another facial picture was used as a hard distractor. Following this, the participant was shown another facial picture, having to then conclude whether this face was the same as the first. The Karolinska Directed Emotional Faces of both female and male faces were used as the facial pictures. Characteristic features such as hairline were removed and the pictures were modified to be as neutral as possible. Facial characteristics remained unmodified. A total of 240 pictures of faces were shown in four blocks with 60 pictures in each block. Reaction times and the proportion of correctly identified faces were used as behavioral measures. First, a fixation cross was shown (1000 milliseconds), followed by the encoding picture (500 ms), and another fixation cross (2000 ms). After the second fixation cross, participants saw the distractor picture (500 ms), a fixation cross (1000 ms), and the retrieval picture (500 ms). Lastly, a question mark (max. 2000 ms) was shown and the participants answered to the task. The progression of the cognitive task is depicted in Image 1.

IMAGE 1. Cognitive Task with Difficult Distractor Picture.

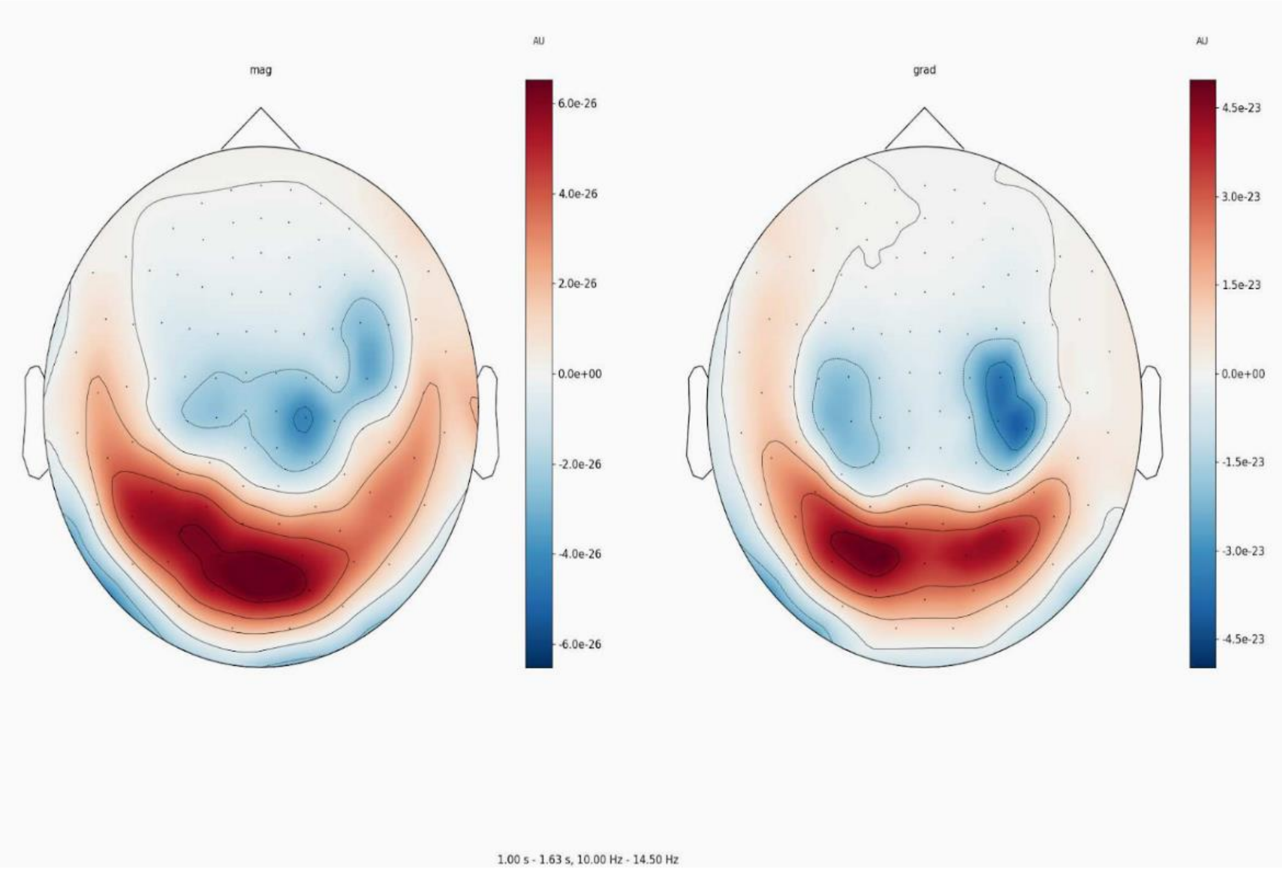
+		+		+		**?**
Fixation cross	Encoding picture	Fixation cross	Distractor picture	Fixation cross	Retrival picture	Question mark
1000 ms	500 ms	2000 ms	500 ms	1000 ms	500 ms	2000 ms

2.5 MEG Data Analysis

Ongoing oscillatory brain activity was recorded. This study focused on the changes in power of alpha oscillations. The data was preprocessed with Maxfilter 3.0 to filter out noise caused by external distractors, such as head movement and air conditioning. Virtual transform for head positions was controlled to transform the heads of the participants to the same co-ordinates. Independent Component Analysis (ICA) was used to remove artefacts caused by eye movements and heartbeat. After the ICA analysis, data was epoched to focus on certain periods of time, and to analyze them separately from the rest of the data. Epoching was conducted in respect to the distractor image; including the time period for the coding picture before the distractor image, and the time period after the distractor image. Averages were calculated for each category. This allowed for comparison of the induced responses and the changes in alpha power during the course of each stimulus. An epoch started 2400 milliseconds before participants saw the encoding picture, and ended 2400 milliseconds after participants saw the last picture.

In order to specify inhibition-related brain areas, time-frequency representation (TFR) analysis was used to detect those areas of the brain which showed the strongest alpha responses during a cognitive task, i.e. were needed for inhibitory processes. According to the TFR analysis, the occipital cortex showed the strongest activation during an inhibitory task. The frontal cortex was also selected for further analysis since the frontal areas are known to be involved in inhibitory processes. Following this, temporal spectral evolution (TSE) analysis was used in order to focus on the modulation of alpha-band oscillations over time.

IMAGE 2. Over subject topographic map of alpha band; group mean from baseline MEG measurement based on TFR analysis.



2.6 Statistical Analysis

Microsoft Excel was used to calculate averaged power of occipital and frontal alpha for each MEG channel of each individual. Statistical analysis was performed using SPSS Statistics. First, the test of normality was used to confirm that sample means were normally distributed. A repeated measures ANOVA was used to analyze differences in alpha modulation between the two intervention groups in three factors; hemisphere, time, and location (i.e. the frontal or the occipital lobe).

Descriptive statistics of the total number of errors made in Stroop test and Trail Making Test A and B were observed. Only the third part of Stroop test was used since it is the most challenging one with incongruent ‘color’ words and ink colors. The number of errors made in Trail Making Test A was small and ranged from zero to one, therefore no further analysis was made for this part of the test. Differences in performance in Stroop test and Trail Making Test B were analyzed with a repeated measures ANOVA, between the baseline measurement and the 12-month follow-up and the intervention groups. The total number of errors was used to describe cognitive performance. The Mann-Whitney U test was also used to confirm the results of the repeated measures ANOVA in alpha modulation and performance in cognitive tasks, since the data was not completely normally distributed.

3. RESULTS

Table 1. depicts the results of the repeated measures ANOVA for analyzing modulation. There were no significant differences between the two times the measurements were performed. Additionally, the intervention groups did not differ from each other significantly. There was no difference in alpha reactivity to distracting stimuli between the two hemispheres. Significant differences in alpha modulation during an inhibition task was found between the frontal and occipital lobes ($F(1) = 43.21$, $p<0.001$), and pairwise comparisons (Table 2.) showed stronger alpha power in the occipital lobe.

TABLE 1. Differences in alpha modulation between time, location, hemisphere and intervention group.

	df	F	sig.
Time	1	.773	.389
Time*intervention group	1	.745	.397
Location	1	43.214	.000***
Location*intervention group	1	2.569	.123
Hemisphere	1	.472	.499
Hemisphere*intervention group	1	.531	.474

***p<,001

TABLE 2. Differences in alpha power in occipital (1) and frontal (2) lobe

(I) location	(J) location	Mean Difference (I-J)	Std. Error	Sig. b	95% Confidence Interval for Difference b Lower Bound	Upper Bound
1	2	2.117*	.322	.000	1.449	2.785
2	1	-2.117*	.332	.000	-2.785	-1.449

Based on estimated marginal means
*. The mean difference is significant at the ,05 level.
b. Adjustment for multiple comparisons: Bonferroni.

We confirmed the reliability of the results of the repeated measures ANOVA by using the Mann-Whitney U test. No differences in alpha modulation between the two intervention groups were observed in the left occipital cortex (U = 68, p = 0.931), the right occipital cortex (U = 50, p = 0.259), the left frontal cortex (U = 58, p = 0.508) or the right frontal cortex (U = 47, p = 0.192).

Descriptive statistics showed that the mean number of errors in Stroop test was 2.46 (Median = 1) at the baseline and 1.71 (Median = 1) at the 12-month follow-up evaluation. The mean number of errors in Trail Making Test B was 0.63 (Median = 0) during the first assessment, and 0.71 (Median = 0) 12 months later. In Stroop Test, the repeated measures ANOVA showed a nearly statistically significant difference (p = 0.085) between the baseline measurement and the 12-month follow-up assessment, but the difference was not seen when compared between the intervention groups. No significant differences were found between the measurement times or intervention groups in Trail Making Test B. The results are shown below in Table 3.

TABLE 3. Differences in number of errors in Stroop test and Trail Making Test B between time and intervention group

	df	F	sig.
STROOP TEST			
Time	1	3.245	.085
Time*intervention group	1	1.600	.219
TRAIL MAKING TEST B			
Time	1	0.002	.964
Time*intervention group	1	1.768	.197

The results of cognitive performance were confirmed by using the Mann-Whitney U test, since some issues were observed in the normal distribution of the data. No significant differences in the group performance means between the two intervention groups were observed in Trail Making Test B ($U = 55$, $p = 0.403$) or the Stroop Test ($U = 92.5$, $p = 0.192$).

4. DISCUSSION

This thesis aimed to study the effects of a one-year physical intervention and combined physical and cognitive intervention on the inhibitory functions and cognitive performance of older adults, investigating whether the effects would be greater in the combined physical and cognitive intervention group. It was assumed that an increase in alpha power during distracting stimuli in a visual working memory task would reflect enhanced inhibition, and that the enhanced inhibition would result in better performance in cognitive tests.

Conflicting with earlier research, physical intervention did not improve performance in the inhibitory or working memory tasks. Physical intervention did not affect the power of alpha oscillations either. Furthermore, our expectations were that a combined one-year intervention would improve inhibitory functions more than a physical intervention alone, and that this would be seen in the power of alpha oscillations. Contrary to our expectations, a combined intervention did not show significant effects on the power of alpha oscillations, thus there were no differences in the effects between the two intervention groups. Nonetheless, statistical analysis showed stronger alpha power in the occipital area in comparison to the frontal area, indicating that the occipital area has an important role in inhibitory functions during visual working memory tasks. Although the location of the alpha power during inhibitory and working memory tasks was not among our uppermost interests, these results are consistent with earlier studies where alpha activity has been detected to increase in the occipital area during the processing of distracting stimuli (Bonnefond & Jensen, 2012).

Our expectations that a combined intervention would be more effective in increasing cognitive test performances in comparison to a physical intervention alone, did not gain support either. There was a nearly statistically significant effect within the groups when we analyzed the number of errors made in Stroop test, indicating that participants showed slightly increased cognitive performance after the intervention. However, when we compared the effects between the two intervention groups, we discovered no significant differences, which indicates that the type of intervention did not correlate with better performance in inhibitory tasks. Participants in the PTCT group practiced Stroop number task, which may have resulted in a better performance of the PTCT group in Stroop word test as well. Interestingly, when we compared these two groups according to their performances in the baseline assessment, we discovered that participants in the PTCT group already showed less errors in Stroop test and Trail Making Test at the beginning of the study. Therefore, we may assume that the cognitive performance of the participants in the PTCT group was already higher than of the participants in the PT group. Additionally, the overall number of errors made in the cognitive tests was small, with the majority of the participants making only one or no errors. It is possible that the cognitive capacity of the participants was good, and more variation in the number of errors may have been detected with different cognitive tests. Due to the small number of errors made in the cognitive tests, these results should be considered critically.

Earlier studies have proven physical exercise to have a positive effect on certain neural conditions which are crucial for cognitive performance and development in older adults, for example brain volume and vascular plasticity (Maass et al., 2015; Erickson et al., 2011). It is possible that by using indicators measuring metabolic and structural changes of the brain we may have distinguished effects related to physical exercise.

Since previous research has shown physical and cognitive intervention to be effective in increasing activity of the brain among older participants, it is surprising that there were no significant differences in cognitive performance, even though both of our intervention groups participated in a one-year physical intervention (Colcombe et al., 2004). Long-term training programs have been proven to be the most effective in comparison with moderate and short-term training programs (Colcombe & Kramer, 2003). Earlier research on this topic have varied in their focus and methods, and the effects of physical or cognitive exercise on alpha modulation has not been widely examined. A lack of research on the focus of our study makes comparing our results to other studies challenging and emphasizes the need for further research.

It is important to note that this study was carried out with an ageing population only. Conversely, Borghini et al. (2018) and Volf and Gluhih (2010) have studied the changes in alpha rhythms by comparing two groups; younger and older participants, and noticed ageing-related differences between the two groups. It is possible that by using groups of older and younger participants we could have compared whether the interventions had age-related effects. For example, Hillman, Erickson and Kramer (2008) discovered that physical exercise had stronger effects on psychomotor speed among elderly participants than younger participants. The researchers concluded that physical exercise may have a more specific effect on participants of different ages.

Furthermore, in some studies a control group of inactive participants has been used in order to distinguish the effects of physical activity alone (Colcombe et al., 2004). It is also of significance that most of the participants were women, which may have affected the results, since women are known to be less vulnerable to ageing-related cognitive decline than men, and studies have shown that ageing women usually perform better in most cognitive tests (Exel et al, 2001; McCarrey et al., 2016). Moreover, since the PTCT group already had a higher level of performance in the cognitive tasks at the baseline assessment, it is possible that individuals with higher cognitive capacity had been unintentionally selected for the PTCT group.

Even though physical and cognitive exercise are known to be effective ways to prevent ageing-related cognitive decline, it is not yet completely known what type of intervention is the most effective to enhance cognitive abilities. There are both human and animal studies that emphasize the role of aerobic exercise in being the key component for brain health (Erickson et al., 2011; Nokia et al., 2016). However, there are conflicting results between different studies, as some of the research shows that combined aerobic and anaerobic exercise intervention is more efficient than aerobic exercise intervention alone (Colcombe & Kramer, 2003). Some studies claim that both single aerobic or anaerobic exercise combined with cognitive intervention have an impact on cognitive skills when compared to physical or cognitive interventions alone (Lauenroth, Ioannadis & Teichman, 2016). Forte et al. (2013) discovered that multicomponent training and progressive resistance training improved older adult participants' inhibitory functions in cognitive tests, independent of the training program. However, multicomponent training seemed to improve inhibition directly, whereas resistance training affected inhibition through improved muscular strength. Rahe et al. (2015) on the other hand distinguished that both cognitive and combined cognitive and physical training interventions increased performance in cognitive tasks, indicating that physical exercise is not necessarily essential in contributing to the effects of cognitive intervention. According to these conflicting results between different studies, the effectiveness of combined cognitive and physical interventions remains yet somewhat unclear.

Additionally, besides paying attention to the type of exercise intervention, there is also a possibility that potential cognitive improvement caused by cognitive intervention depends on the degree of difficulty of the intervention. Since we did not find any intervention group related evidence of cognitive improvement, one conclusion may be that the cognitive training program in this study was not challenging or intensive enough to improve the cognitive skills of the participants. Furthermore, it is worth considering whether the cognitive training program used was particularly focused on improving inhibitory and working memory functions and not some other cognitive skills.

Even though we did not find any significant differences between the PT and the PTCT intervention groups according to cognitive performance or changes in alpha power, these results highlight the need for further research on this particular topic, as different studies have produced conflicting results.

Furthermore, enhancing brain functions and cognition via physical and cognitive activity may have more extensive effects on the experienced quality of life. Physical and cognitive activity contribute independent living and moreover, moderate and high levels of physical activity has been found to decrease the risk for Alzheimer's disease and dementia (Oswald, Gunzelmann, Rupprecht & Hagen, 2006; Laurin et al., 2001). Additionally, physical and cognitive training has been discovered to be effective in enhancing higher levels of cognitive and physical functioning, but also lower levels of depressive symptoms (Oswald, Gunzelmann, Rupprecht & Hagen, 2006). Moreover, since the prevalence of cognitive impairments among elderly populations will likely become more considerable in the future, finding ways to prevent cognitive decline is widely relevant for both individuals and society at large (Deary et al., 2009; Suthers, Kim & Crimmins, 2003).

4.1 Limitations

There are some limitations in our study that need to be considered when drawing a conclusion of the results. First of all, our sample size was relatively small. It is possible that with a bigger sample size there may have been more distinguishable effects. Secondly, the majority of the participants were women, thus the sample may not have accurately reflected the general population. Additionally, participants were selected by asking for volunteers from the PASSWORD Project to take part in t brain study. It is possible that the voluntary participants had better cognitive skills to start with, or a higher interest in training their cognitive skills compared to a random sample, which may have affected the results.

To study the differences between the effects of physical and cognitive exercise, a group attending cognitive intervention only should have been included to this study. For more reliable comparisons between different intervention types, it would have also been essential to have a control group that did not participate in physical or cognitive exercises. Furthermore, participants were also given an opportunity to conduct their intervention programs independently, hence it is not possible to know for certain if they complied with the program completely according to the instructions. It is also possible that the procedure used to measure inhibition and working memory was actually focused on some other cognitive functions and not the ones we were interested in.

4.2 Future Studies

Conflicting with earlier research, our study did not show any evidence that combined physical and cognitive intervention increased cognitive performance more than physical intervention alone.

However, these results point out that more research focusing on the effects of different types of interventions on cognitive abilities among ageing population is needed.

Yet there is currently only limited research on how physical and cognitive interventions affect alpha oscillations. Since we did not find any relation between combined intervention and alpha modulation, more research on this subject is needed. Additionally, to specify how exactly oscillatory functions of the brain are affected by physical and cognitive intervention, it would be essential to study other oscillations as well. In addition, since some studies have shown that combined interventions have differing effects on younger participants compared to older participants, more studies on how the power of alpha oscillations is affected by interventions in different age groups would help to further illuminate the characteristics of alpha oscillations.

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