RELATIONSHIP BETWEEN PHYSICAL ACTIVITY, FITNESS AND BRAIN MORPHOLOGY IN YOUTH

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Growing evidence has displayed a relationship between physical activity, fitness and cognitive functions, yet the underlying mechanisms and changes in brain morphology explaining this connection are still quite unknown. The current study examined whether physical activity or physical fitness is related to regional brain volume or cortical thickness in youth. The subjects were 35 Finnish adolescents (14.14 ±0.71 years, 23 females & 12 males), a subsample from Active, Fit and Smart (AFIS) – research project. Measurements included objective physical activity measurement with accelerometers, physical fitness test battery and brain imaging procedure with magnetic resonance imaging (MRI). From the larger study sample of the AFIS – research project, two groups were formed based on the physical activity measurements, active (n=18) and non-active (n=17). The active group included the most physically active subjects, measured as the average daily time involved in moderate-to-vigorous activity, and the non-active group included the most inactive subjects. The relationship between physical activity and brain morphology was examined by comparing the two groups using the analysis of covariance, controlling the effect of age, puberty status and body mass index. The relationship between physical fitness and brain morphology was examined by looking at correlations between the physical fitness tests and chosen brain variables. It was found, that physical activity had a positive relationship with the thickness of the right parahippocampal cortex [$F(1, 30)=4.44$, $p<0.05$)]. Physically more active subjects expressed a thicker right parahippocampal cortex compared to less active subjects. A relationship was also found between physical activity and the thickness of the left paracentral cortex, yet this finding lost significance after controlling the effect of age [$F(1, 30)=2.50$, $p=0.12$)]. Physically more active subjects expressed a thicker left paracentral cortex than less active subjects, whereas older subjects expressed a thinner left paracentral cortex compared to younger subjects. No other brain region displayed a connection with the level of physical activity and no significant correlations were detected between different components of physical fitness and the brain variables. These findings imply that the area of right parahippocampal cortex might be especially susceptible to physical activity induced changes in youth, and that physical activity does not necessarily have to improve physical fitness to cause changes in brain morphology.

Keywords: Brain volume, cortical thickness, physical activity, physical fitness,

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Yhä useammat tutkimukset ovat havainneet yhteyden fyysisen aktiivisuuden, fyysisen kunnon ja kognitiivisten kykyjen välillä, mutta tätä yhteyttä selittävät tekijät ja siihen liittyvät muutokset aivojen rakenteissa ovat vielä varsin epäselviä. Tässä tutkimuksessa oli tarkoitus selvittää, onko fyysisellä aktiivisuudella tai fyysisellä kunnolla yhteyttä aivojen rakenteeseen nuorilla. Tutkimuksen koehenkilöt olivat 35 suomalaista nuorta (14.14 ±0.71 vuotta, 23 tyttöä & 12 poikaa), otanta laajemmasta AFIS (Active, Fit and Smart) -tutkimusprojektista. Tutkimuksessa mitattiin fyysistä aktiivisuutta objektiivisilla kiihtyvyysanturimittareilla, fyysistä kuntoa lasten ja nuorten mittaamiseen tarkoitetulla kuntotestipatteristolla sekä aivojen rakennetta magneettikuvantamisen avulla. AFIS -tutkimusprojektin suuremmasta koehenkilömäärästä muodostettiin kaksi ryhmää fyysiseen aktiivisuuteen perustuen, aktiiviset (n=18) ja passiiviset (n=17). Aktiivisuus määriteltiin keskimääräisenä päivittäisenä aikana, joka vietettiin keskiraskaalla tai raskaalla aktiivisuustasolla. Fyysisen aktiivisuuden yhteyttä aivojen rakenteeseen tutkittiin vertailemalla näitä kahta ryhmää keskenään kovarianssianalyysin avulla, kontrolloiden iän, puberteetin vaiheen sekä painoindeksin vaikutus. Fyysisen kunnon yhteyttä aivojen rakenteeseen tarkasteltiin kuntotestien tulosten sekä valittujen aivoalueiden välisillä korrelaatioilla. Tutkimuksessa havaittiin fyysisellä aktiivisuudella olevan positiivinen yhteys oikean parahippokampaalisen korteksin paksuuteen [$F(1, 30)=4.44$, $p<0.05$)]. Fyysisesti aktiivisilla henkilöillä oikea parahippokampaalinen korteksi oli paksumpi verrattuna vähemmän aktiivisiin henkilöihin. Fyysisellä aktiivisuudella havaittiin myös yhteys vasemman parasentraalisen korteksin paksuuteen, mutta tämän yhteyden merkitsevyys katosi iän kontrolloimisen myötä [$F(1, 30)=2.50$, $p=0.12$)]. Fyysisesti aktiivisemmilla henkilöillä vasen parasentraalinen korteksi oli paksumpi kuin vähemmän aktiivisilla henkilöillä, mutta vanhemmilla koehenkilöillä korteksi oli ohuempi kuin nuoremmilla. Mikään muu tutkittu aivoalue ei ilmentänyt yhteyttä fyysisen aktiivisuuden kanssa, eikä mikään fyysisen kunnon osa-alue ja tutkittujen aivoalueiden välinen korrelaatio saavuttanut merkitsevää tasoa. Tulokset viittaavat parahippokampaalisen korteksin olevan erityisen altis fyysisen aktiivisuuden aiheuttamille muutoksille nuoruudessa. Lisäksi tuloksista voidaan päätellä, ettei fyysisen aktiivisuuden tarvitse välttämättä kohottaa fyysistä kuntoa, jotta aivojen rakenteessa voi tapahtua muutoksia.

Avainsanat: Aivojen volyymi, kortikaalinen paksuus, fyysinen aktiivisuus, fyysinen kunto

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CONTENTS

1 INTRODUCTION

Regular physical activity is widely known to improve our physical health and well-being, yet growing evidence shows it can improve our brain function and cognitive skills as well (Hillman, Erickson & Kraemer, 2008). Although animal studies have already suggested some possible mechanisms, very little is still known about the structural brain changes underlying the cognitive benefits achieved with exercise, especially in humans (Yau, Gil-Mohapel, Christie & So, 2014). The increasing inactivity among youth is concerning, as the amount of children and adolescents fulfilling the guidelines for physical activity decreases steadily with age. While about 40 % of primary school aged children are active the recommended one hour daily, only a third of 13-year-olds, and not even a fifth of 15-year-old Finnish students fulfill this recommendation. Physical activity clearly decreases during adolescence. (Kokko et al., 2016).

Physical activity has shown to be beneficial for brain functioning, at least in adults and elderly. It seems also that regular physical activity and aerobic fitness are positively correlated with academic achievements in children. (Guiney & Machado, 2012). Also the hippocampal volume has shown to be larger and memory functioning to be better in highly fit children compared to lower fit ones (Chaddock et al., 2010). In addition to aerobic fitness, also strength and motor skill learning have shown to have a positive relationship with certain brain areas (Anstey et al., 2007; Gryga et al., 2012; Koppelmans, Hirsiger, Mérillat, Jäncke & Seidler, 2015).

During childhood and adolescence, the brain is the most plastic and develops rapidly. From childhood towards maturity and adulthood, the brain structure changes. For example, the white and gray matter volumes and neural connections change throughout childhood up to young adulthood. (Gogtay et al., 2004). Since the brain is the most plastic in childhood and youth, also the external influences can have a great impact on brain development at early age. If physical activity causes beneficial changes to brain structure and function, lack of physical activity in youth might therefore have negative effects on cognitive functions, in addition to the negative effects on physical well-being. (Herting & Nagel, 2012; Voss, Nagamatsu, Liu-Ambrose & Kramer, 2011). As growing evidence shows that physical activity benefits brain health and cognition in older individuals, more research is needed to assess the similar connection in youth (Herting & Nagel, 2012).

1.1 Brain areas and cognitive functions susceptible to physical activity

Physical activity does not seem to influence all brain regions similarly. It has been noticed, that while some brain areas are more susceptible to exercise, other brain regions show minimal or no change followed by physical training. (Erickson et al., 2011). By influencing in only specific brain areas, physical activity seems to cause selective improvement in cognitive functions. Although some studies suggest comprehensive cognitive benefits due to physical activity, several previous studies have found physical activity to improve primarily executive functions and hippocampal dependent memory functioning (Erickson et al., 2011; Erickson, Leckie & Weinstein, 2014; Flöel et al., 2010; Hillman, Castelli & Buck, 2005; Voss et al., 2011).

It has been hypothesized, that physical activity affects cognitive functions and brain areas mostly during the time, when they undergo developmental changes, thus age might be a moderating factor in the relationship between physical activity and brain health. Frontal brain regions mature late in adolescence, which might make them more sensitive to own activity dependent external factors, like physical activity, compared to mature structures. (Hötting & Röder, 2013). Late maturation of the frontal regions explains also the relatively late development of executive functions, which are thought to be subserved by the frontal lobes. These functions refer to higher level cognitive processes, such as planning, self-regulation, initiation, inhibition and cognitive flexibility. (Verburgh, Königs, Scherder & Oosterlaan, 2014). In addition, frontal brain regions are especially prone to age-related deterioration, explaining the benefits of physical activity to those areas also in older population (Hötting & Röder, 2013).

Along with the frontal lobes and executive functions, also the hippocampus and several memory functions seem to express beneficial changes due to physical activity. Studies in both animals and humans have discovered positive changes in the hippocampal area as a result of aerobic exercise. (Erickson et al., 2011; Erickson et al., 2014; Nokia et al., 2016). Hippocampus (Figure 1), a part of the medial temporal lobe, is one of the most important brain structures involved in memory and learning (Shohamy & Turk-Browne, 2013). Hippocampus has been linked to various important cognitive functions, such as creating novel memories, retrieving specific episodic memories, context dependent learning and also spatial memory (Erickson et al., 2011; Reber, 2013; Yau et al., 2014). In older adults, the hippocampal volume has been noticed to shrink approximately 1–2% a year, showing significant age-related deterioration similar to the frontal brain regions (Erickson et al., 2011). However, Erickson et al. (2011) discovered, that physical activity might be an effective way to decelerate the degradation, or even increase hippocampal volume. Moreover, aerobic exercise has been linked to larger hippocampal volumes in adolescents (Herting & Nagel, 2012), as well as preadolescent children (Chaddock et al., 2010). In conclusion, the hippocampus seems to be one of the brain areas in which physical activity can bring positive changes throughout lifetime. (Erickson et al., 2014; Herting & Nagel, 2012; Killgore, Olson & Weber, 2013).

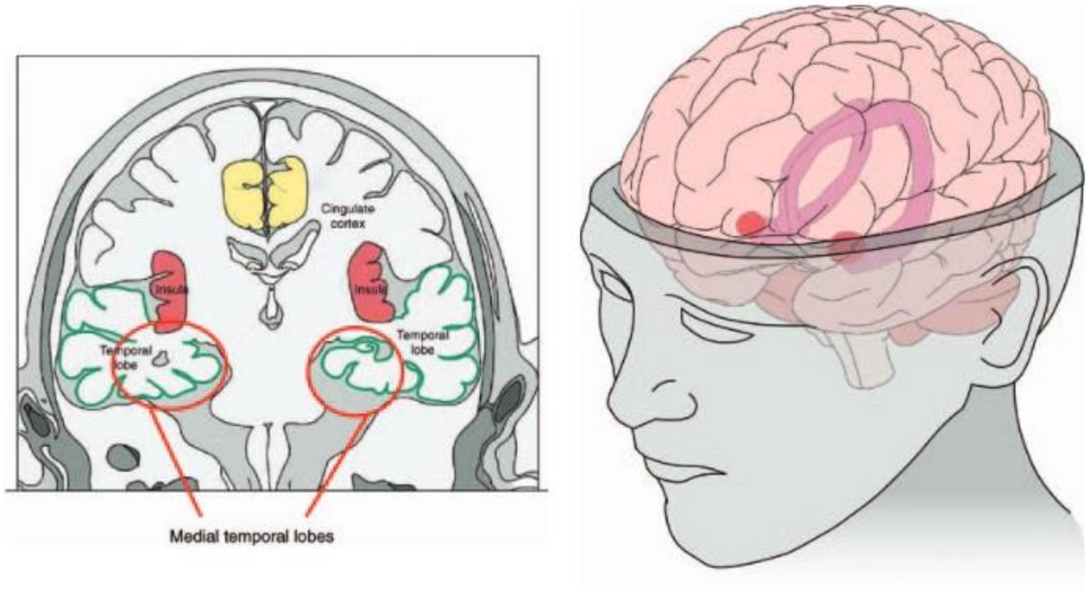

FIGURE 1. The location and anatomy of the medial temporal lobe and hippocampus (Baars & Gage, 2010, 306).

However, despite of promising discoveries from animal studies, the results on the topic in humans is still lacking consistency (Hötting & Röder, 2013). Not all studies have established a relationship between physical activity and brain volume, and some studies have also noticed the significant relationship disappear, when a moderating factor, such as age, stress or body mass index (BMI) is taken into account. (Erickson et al., 2014). Nonetheless, a clear majority of the studies reported in the comprehensive review by Erickson et al. (2014), looking at the relationship between physical activity and brain volume, reported physical activity or fitness to have an effect on the prefrontal and/or hippocampal volumes. Although the consistency of the results varies and the mechanism of how physical activity and fitness can increase brain volume is not clear, the evidence is still promising.

1.2 Effects of aerobic, resistance and motor skill training on brain morphology and cognitive functions

Besides physical activity, also exercise and physical fitness have shown to have an effect on brain anatomy and functioning (Voss et al., 2011). Although closely related, the terms physical activity and physical exercise must be considered as independent variables. Physical activity can be defined as bodily activity that increases energy expenditure above resting levels, whereas physical exercise refers to more organized training with the intension of improving physical fitness (Thomas, Dennis, Bandettini & Johansen-Berg, 2012). There have been controversial results, whether the effects of physical activity on brain volume and function are independent, or moderated by some physiological factor, such as aerobic fitness. (Colcombe et al., 2004; Flöel et al., 2010). However, whether studying either the effect of physical activity or aerobic fitness on brain structure and function, they both seem to cause similar outcomes and have specific effects on the same brain areas (Erickson et al., 2014).

Like physical activity, also aerobic exercise has shown to have an effect predominantly in executive functions. Studies have shown the frontal and prefrontal brain region volumes to increase after aerobic exercise, at least in older individuals (Colcombe et al., 2006; Erickson et al., 2014). In addition, the ability to activate the frontal brain regions and therefore perform better in tasks requiring high level of cognitive control has been noticed to be better in higher-fit children (Chaddock et al., 2012). Along with frontal regions, aerobic fitness seems to benefit the hippocampal region as well. Erickson et al. (2011) established in their study, that higher-fit adults had bigger hippocampal and medial temporal lobe volumes, and that aerobic training increased hippocampal perfusion. It was also discovered, that the more the aerobic fitness was improved, the more the hippocampal volume increased as well (Erickson et al., 2011). Similar results have also been established among younger subjects. Aerobic fitness has been noticed to correlate with hippocampal volume in adolescents (Herting & Nagel, 2012) and larger hippocampal subfields have correlated positively with episodic memory functions in youth (Lee, Ekstrom & Ghetti, 2014).

Most studies on the field have focused on exploring the influence of aerobic exercise on brain anatomy and functioning, yet also resistance training and coordination training have been noticed to alter the brain structure and possibly enhance cognitive functions as well (Bherer, Erickson & Liu-Ambrose, 2013; Hötting & Röder, 2013). For example, Koppelmans et al. (2015) found a correlation between grip strength and contralateral gray matter cerebellar volumes, as well as motor cortex volume, when studying healthy older adults. Some evidence supports also the relationship between grip strength and white matter volume (Kilgour, Todd & Starr, 2014). In addition, resistance training has shown to improve executive functions, short-term memory and attention in older individuals. Animal studies have also provided a link between resistance training and spatial memory. (Hötting & Röder, 2013). The link between resistance training, brain health and cognitive functions is, however, still very unclear, and no previous studies have focused on examining the topic on children or youth. (Voss et al., 2011).

Finally, also motor skills and skill training have displayed a connection with brain structure and functioning. Especially motor-related brain regions have expressed gray matter increases after motor skill learning, yet structural changes have also been noticed outside the motor cortex. Gryga et al. (2012) found a bidirectional connection between gray matter volume and motor skill learning abilities. In their study, gray matter volume increased the most in individuals acquiring the motor skill well, yet also the initial level of gray matter volume predicted how well the introduced motor task would be learned (Gryga et al., 2012). In addition to gray matter changes, motor skill training has been linked to white matter changes as well. For example, Scholtz, Klein, Behrens and Johansen-Berg (2009) found regional white matter volume increases after training for complex visuo-motor task. These results imply, that also motor skill training can cause changes in brain morphology, including areas outside the primary motor cortex.

1.3 Plasticity of the brain

Neuroplasticity refers to the ability of the brain and its neural circuits to adapt to new challenges and environments. For example, learning can induce changes in the neurotransmitters and their release, which might eventually lead into structural brain changes as well. In addition to learning, also behavioral and environmental factors can either facilitate or hinder neuroplasticity. (Hötting & Röder, 2013). For example aging, stress and drug use have been noticed to deteriorate neural plasticity (Khan & Hillman, 2014; Konrad, Firk & Uhlhaas, 2013). On the other hand, factors noticed to improve neuroplasticity include special types of dietary habits, medical treatments, enriched environments, cognitive stimulation and physical exercise (Hötting & Röder, 2013). Along with the brain structure, also the plasticity of the brain seems to have a significant role considering intelligence (Schnack et al., 2015).

The brain can express changes in both gray and white matter volumes and structures. Possible mechanisms explaining these changes include neurogenesis, changes in neuronal morphology, vascular changes, changes in glia cell number and size, myelination or axonal changes.

Neurogenesis refers to the formation of new neurons, yet it is an unlikely explanation for brain structure changes outside the hippocampus, one of the only brain areas new neurons have been noticed to originate. However, other plausible neuronal morphology changes include, for example, synaptogenesis, the formation of new synapses between neurons and dendritic spine formation. The vasculature of the brain can also express plasticity, and it has been discovered in both animals and humans, that exercise can increase the blood volume in the dentate gyrus of the hippocampus. (Zatorre, Fields & Johansen-Berg, 2012). Aerobic fitness has also been linked to higher blood flow velocity of the middle cerebral artery, indicating global cerebral blood perfusion, thus suggesting superior cerebrovascular functioning in higher-fit individuals (Guiney & Machado, 2012). Animal studies have also discovered exercise-induced increases in angiogenesis, the creation of new blood vessels in the brain. Angiogenesis has been noticed to take place in the hippocampus and also in areas involved in executing voluntary movements, like the cerebellum and the primary motor cortex. Interestingly, these findings are limited to young animals only, whereas no changes in angiogenesis have been found in aged animals. (Voss et al., 2011).

Changes in white matter can be explained with either myelination or axonal modifications. Myelination continues linearly up to young adulthood (Houston, Herting & Sowell, 2014), yet behavioral factors have also been noticed to influence the process (Zatorre et al., 2012). White matter changes can also be due to modifications in axon diameter or permeability (Zatorre et al., 2012). In addition to changes in gray or white matter, external factors can induce changes also in the levels of growth factors or neurotransmitters. For example, physical activity has been noticed to increase the release of brain-derived neurotrophic factor (BDNF) and insulin-like growth factor (IGF-1) and also to elevate the levels of serotonin, noradrenaline and acetylcholine. These have also been noticed to play an important role in neuroplasticity. (Hötting & Röder, 2013).

1.4 Brain development in youth

The brain changes drastically both anatomically and functionally during childhood and adolescence. Certain parts of the brain can reach maturity already in early childhood, but some regions develop even up to early adulthood. For example, the sensory regions have been noticed to achieve maturity already by the age of seven, while the prefrontal cortex keeps developing throughout the entire childhood, explaining also the late development of executive functioning in children. (Khan & Hillman, 2014). To examine reliably the effects of external influences, such as physical activity, to brain morphology in youth, it is highly important to consider the developmental changes occurring in the adolescent brain.

Brains are highly individual in their size, shape and structure. Although previous studies have suggested that, for example, total cerebral volume and both gray and white matter volumes are mainly determined by genes and therefore highly heritable, some brain areas and their development have shown to be almost entirely mediated by environmental factors. It has been suggested, that the earliest stages of brain development are mostly mediated by genetic effects, whereas later stages of brain development involve a much more complex interaction from both genetic and environmental influences. (Baare et al., 2001; Yoon, Fahim, Perusee & Evans, 2010). For example, the frontal and temporal gray matter structures seem to be less mediated by genetic, yet increasingly mediated by environmental factors with age (Wallace et al., 2006). Since the brain undergoes such great changes during childhood and adolescence, and is highly sensitive to environmental influences at that time, a physically active lifestyle during that period might influence the brain development positively, and therefore improve cognitive capacity as well (Herting & Nagel, 2012).

Total brain volume has been noticed to increase steadily up to the age of 13, from where it starts to gradually decrease (Hedman, Van Haren, Schnack, Kahn & Hulshoff Pol, 2012). During adolescence, the gray matter volume has been noticed to decrease, whereas white matter volume seems to increase up to early adulthood. Changes in gray matter are thought to be due to synaptical pruning, the elimination of unused neural connections and changes in white matter due to myelination. (Konrad et al., 2013). In addition, the greatest changes regarding cortical thinning seem to occur during adolescence (Tamnes et al., 2010). The hippocampal volume has been noticed to increase up to early adolescence. However, some hippocampal subfields have also been noticed to decrease in volume, and most of the shrinkage seems to appear at mid-adolescence. (Tamnes et al., 2014). Besides age, also pubertal development has been noticed to relate with brain structure changes. It has been suggested, that the hormonal changes occurring in puberty are also influencing structural brain growth. (Goddings et al., 2014). Since both genetic and environmental factors can affect the brain development (Yoon et al., 2010), physically active lifestyle might also have an effect on the process.

1.5 Aims of the current study

The aim of this study was to examine, whether physical activity or physical fitness has a relationship with regional brain volume or cortical thickness in youth. First, the effect of physical activity was examined by comparing brain volume and cortical thickness between active and non-active individuals. Second, the relationship of physical fitness and brain morphology was examined by looking at correlations between different components of physical fitness, brain volume and cortical thickness. Previous studies have shown physical activity and fitness to be linked with increased hippocampal volume (Erickson et al., 2011; Herting & Nagel, 2013; Killgore et al., 2013), the frontal regions (Hötting & Röder, 2013) and the motor cortices (Gryga et al., 2012). However, the results from previous human studies have been established mostly with older individuals, while the number of studies using adolescents as subjects remains extremely limited. The current study is therefore one of the first to link the level of physical activity specifically with brain measures during youth. In addition, the study includes also measures of physical fitness, which have not been linked with brain morphology measures in previous studies with adolescents. The hypothesis for the current study is, that physically more active and more fit individuals show differences in their brain morphology compared to less active and less fit subjects, presumably in the areas of hippocampus, frontal lobes and/or motor cortices.

2 METHODS

2.1 Subjects

The current study is part of Active, Fit and Smart (AFIS) – research project, which examines the effects of physical activity and fitness on the cognitive prerequisites of learning. From the total of 71 subjects taking part in the brain imaging procedure, two groups were formed based on the amount and intensity of daily physical activity (TOTMVPA, total amount of moderate-to-vigorous physical activity). The *'active'* group consisted of the 18 most active students (mean TOTMVPA = 76.3 ±14.7 minutes, f = 10, m = 8) and the *'non-active'* group of the 17 most inactive students (mean TOTMVPA = 31.6 ±6.9 minutes, f = 13, m = 4), who participated in both the physical activity measurement and the brain imagining procedure. The average of daily physical activity (TOTMVPA) for all the subjects with valid activity data was 52.4 ±21.7 minutes. The 35 subjects (18 active & 17 non-active) included in the study were Finnish elementary school students aged 12–15 years (14.14 ±0.71 years, 23 females & 12 males). Out of the 35 subjects, 32 subjects (16 active & 16 non-active) participated in the physical fitness tests, excluding three subjects who did not take part in the tests. The subjects for this study were recruited from the "Finnish schools on the Move" study (FiscMove). Since the subjects were under 18, their parents' consent was requested for participating in the study.

2.2 Study design

The physical activity and fitness measurements were conducted by LIKES research centre. The magnetic resonance imaging was organized by the Department of Psychology of the University of Jyväskylä in collaboration with Aalto University. The magnetic resonance imaging was conducted at the Advanced Magnetic Imaging (AMI) -centre, which is a part of the Aalto Neuroimaging research infrastructure of Aalto University. The brain regions of interest were chosen based on previous literature. Volumetric variables included in the study were the total cortex volume, total gray and white matter volumes and the volumes of the left and right hippocampus. Cortical thickness variables included in the study were the thickness of the left and right hemispheres, areas of the motor cortex (pre-, para- and postcentral cortices), parahippocampal cortices and superior frontal cortices (Figures 2 & 3).

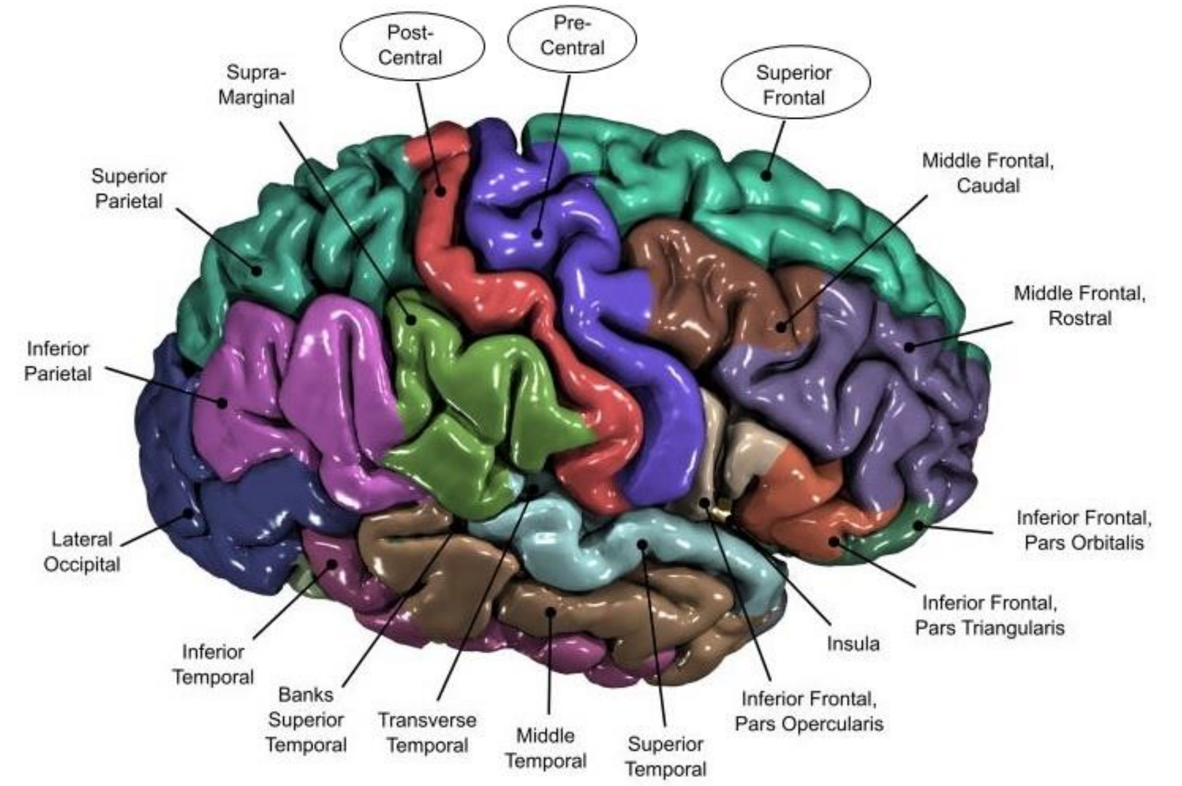

FIGURE 2. Atlas showing the pre- and postcentral cortices and superior frontal cortex. (Modified from Winkler et al., 2010).

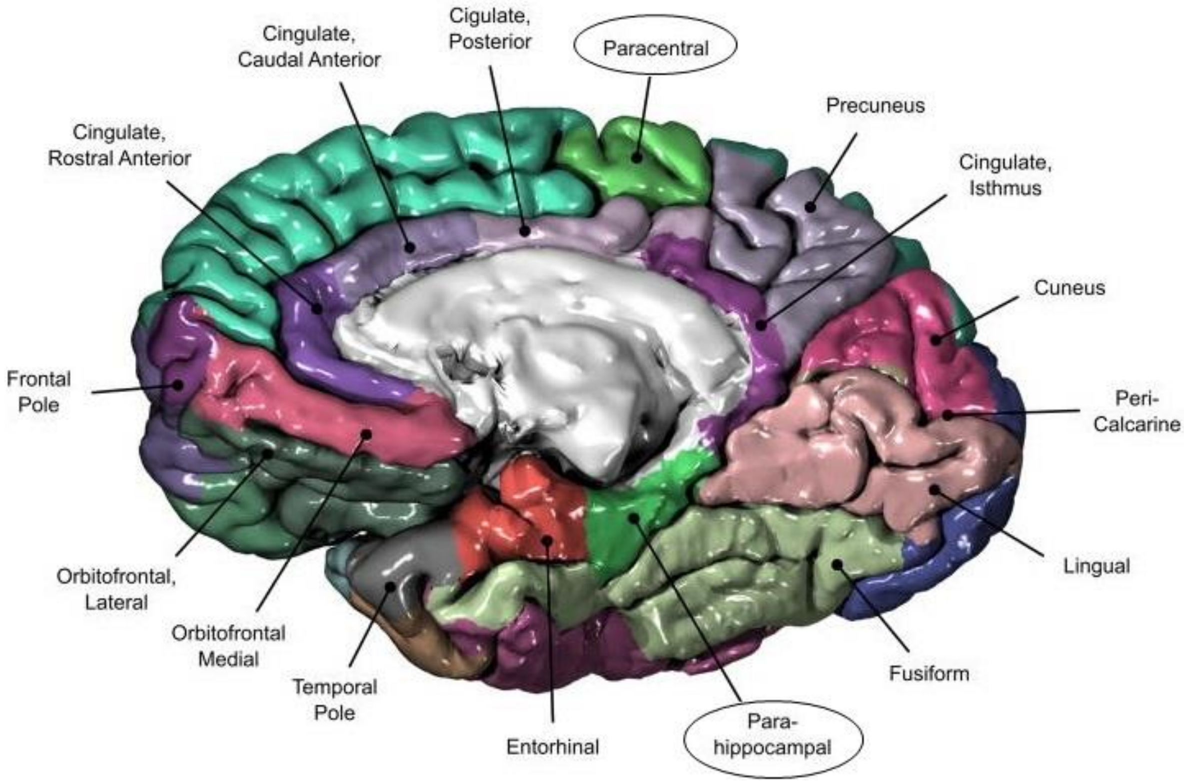

FIGURE 3. Atlas showing the paracentral cortex and parahippocampal cortex. (Modified from Winkler et al., 2010).

2.3 Background measures

Background measures included in the study were age, puberty status and body mass index (BMI) of the subjects. Prior to the brain imagining procedure, the height and weight of the subjects was measured. The BMI was calculated by dividing the bodyweight (kg) with the height (m) squared. The subjects had also filled out a form assessing their puberty status with the Tanner scale, which is a five-stage scale assessing the physical changes occurring with puberty. (Marshall & Tanner, 1969; Marshall & Tanner, 1970). An average from the two questions included in the Tanner scale was used to assess the puberty status.

Previous studies have suggested, that age or BMI might confound the relationship between physical activity and brain morphology (Erickson et al., 2014), so the effect of those variables was controlled in the analysis. In addition, Goddings et al. (2014) found that pubertal development is related to the structural development of subcortical brain regions, and besides age, also puberty status (Tanner scale) is an important factor to be taken into account when studying adolescent brain development. Therefore, the effects of age, BMI and puberty status were controlled in the analysis of the current study.

2.4 Physical activity and fitness measurements

Physical activity measurements. The subjects' physical activity was measured with hip-worn accelerometers (ActiGraph GT3X+) for seven consecutive days. Subjects were advised to wear the accelerometer during the day and only take it off when sleeping or showering. For the analysis, all activity on the levels of moderate-to-vigorous physical activity was combined to form the activity variable (TOTMVPA, total amount of moderate-to-vigorous physical activity). The variable was formed by dividing the total time of moderate-to-vigorous activity by the number of valid measurement days, thus representing the average time of moderate-to-vigorous activity per day.

Physical fitness measurements. The subjects' physical fitness was tested with the *Move!* test battery (Opetushallitus, 2017), which is designed for fitness testing in schools. The test battery consists of six different tests, which measure different components of physical fitness, including aerobic capacity, muscular endurance, power, flexibility and motor skills. From the six tests included in the fitness test battery, five were included in the analysis of the current study, leaving out the mobility test. In addition, the push-up and the upper body lift tests were combined to form a single 'strength' variable for further analysis.

The six tests included in the *Move!* test battery:

1. *20 meter line run:* The 20 meter line run test measures endurance and the level of aerobic fitness. In the test, subjects run 20 meters every time they hear a signal from the test tape. The tempo of the signals increases after every minute. The test result is the time one is capable to run 20 meters repeatedly with increasing tempo. The 20 meter line run has proven to be a reliable and valid test to measure aerobic fitness (Güvenç et al. 2013; Paradisis et al. 2014).

2. *5 continuous jumps*: The 5 continuous jumps test measures strength, power, speed and dynamic balance of the lower limbs. The test is performed by taking five consecutive strides, starting and finishing with joined feet. Test result is the distance covered by these strides.

3. *Upper body lift*: The upper body lift measures the muscular endurance of the abdominal muscles. The test result is the amount of repetitions one is capable to perform in a given tempo. Each repetition must start with head on the ground and heels must remain on the floor. The movement has to be continuous and repetition is accepted, once fingertips touch the measuring tape on the other side. The maximal result for the test is 75 repetitions.

4. *Push-up*: The push-up test measures dynamic strength and endurance of the upper limbs and shoulders. The test is conducted by performing as many push-ups as possible in the time frame of 60 seconds. Hands should be placed at shoulder width and feet cannot be wider than hip width. The movement starts and ends with hands extended. At the bottom position, chest must be lowered to 10 cm off the ground or alternatively touch a 10cm high target. Boys perform the movement with their palms and toes on the ground, girls with their palms and knees on the ground.

5. *Mobility of the body*: The mobility tests measure the body's normal range of motion with three different tests (squat, lower back extension and shoulder flexibility).

6. *Throw-catch combination*: The throw-catch combination test measures handling skills, perceptual motor skills and upper body strength. The test is performed by throwing a tennis ball with one hand towards a specified 1.5m x 1.5m target 20 times and catching the ball after one ground contact. The throwing distance is 10 meters for boys and 8 meters for girls. Subjects are allowed to try the task a couple times before the actual test. The result is the amount of successful throw-catch combinations out of the 20 trials.

2.5 Brain imaging

The magnetic resonance imaging (MRI) was conducted at Aalto University AMI-center, Espoo, Finland. The MR-imaging experiments were performed on a MAGNETOM Skyra syngo MR D13C 3.0T whole-body scanner (Siemens Healthcare, Erlangen, Germany), using a 32-channel head-coil. The maximum field gradient amplitude was 45 mT/m, with slew rate 200 T/m/s. Parent's consent for the imaging procedure was required and all subjects went through a standardized security check routine before scanning. Any contraindications for participating in the study were screened. The scanning took approximately 30–45 minutes and the researcher in charge gave information about the imaging sequences before and during the scanning. Subjects were instructed to keep their head still during the scanning, and pads were used to minimize the head motion. In addition, subjects wore ear plugs to suppress the loud noises of the scanner. All possible disadvantages (i.e. the noisy environment) and the subject's rights were revised before the imaging procedure.

T1-weighted structural images were acquired in sagittal plane using MPRAGE pulse sequence. Protocol included 176 sagittal slices and the scanning time was 6.02 minutes. The acquisition parameters were set as follows: TI = 1100 ms, TR = 2530 ms, TE = 3.3 ms, voxel size = 1.0 x 1.0 x 1.0 mm, flip angle = 7 °, slice thickness = 1mm, FOV = 256 x 256 x 176 mm 3, bandwidth = 200 Hz/Px, and using GRAPPA parallel imaging technique with acceleration factor PE:2 and with 32 reference lines. In addition to the structural images acquired with the MPRAGE pulse sequence, other sequences performed in the brain imagining procedure were the diffusion weighted imaging (DWI), where two sets of 30 diffusion weighted images were acquired with opposite phase encoding directions, resting state fMRI (rs-fMRI), which was obtained for each participant using echo-planar-imaging (EPI) sequence and also arterial spin labeling, using the pulsed arterial spin labeling sequence. The scanning time was 7.47 for each DWI series, 7.05 for the rs-fMRI and 3.57 minutes for the arterial spin labeling.

2.6 MRI data analysis

Cortical reconstruction and volumetric segmentation of the MRI data was performed with the FreeSurfer 5.3 image analysis suite (http://surfer.nmr.mgh.harvard.edu/). The technical details of the procedures are described in prior publications (Dale et al., 1999; Dale & Sereno, 1993; Fischl & Dale, 2000; Fischl, Liu & Dale, 2001; Fischl et al., 2002; Fischl et al., 2004a; Fischl, Sereno & Dale, 1999a; Fisch, Sereno, Tootell & Dale, 1999b; Fischl et al., 2004b; Han et al., 2006; Jovicich et al., 2006; Segonne et al., 2004; Reuter, Rosas & Fischl, 2010; Reuter, Schmansky, Rosas & Fischl, 2012). In short, the processing includes motion correction and averaging (Reuter et al. 2010) of multiple volumetric T1 weighted images, removal of non-brain tissue (Segonne et al., 2004), automated Talairach transformation, segmentation of the subcortical white matter and deep gray matter volumetric structures (including hippocampus) (Fischl et al., 2002; Fischl et al., 2004a), intensity normalization (Sled et al., 1998), tessellation of the boundary of the gray and white matter, automated topology correction (Fischl et al., 2001; Segonne, Pacheco & Fischl, 2007), and surface deformation following intensity gradients to optimally place the borders of the gray and white matter as well as gray matter and cerebrospinal fluid (Dale et al., 1999; Dale and Sereno, 1993; Fischl & Dale, 2000).

After the data had been processed with FreeSurfer, each slice of the MRI images for each subject was checked and fixed manually, if needed. To ensure the skull had been properly cut off from the images, both the watershed-tool and manual erasing of voxels were used. The automated separation of gray and white matter was fixed with control points, if needed. Also the automatic parcellation of the cerebral cortex was checked. From the 37 subjects originally involved in this study, two had to be excluded from further analysis because of the poor quality of their MRI data.

2.7 Statistical analysis

Volumetric and cortical thickness values were imported from FreeSurfer to SPSS Statistics 24, which was used to perform all statistical calculations. An independent samples T-test was used to look at the group differences between the 'active' and 'non-active' groups regarding age, puberty status, height, weight, body mass index (BMI) and the fitness test results. A one-way analysis of covariance (ANCOVA) was conducted to examine the effect of physical activity on brain anatomy, controlling the effect of age, puberty status and BMI. The relationship between physical fitness and the brain variables was examined with Pearson's correlation.

Homogeneity of variances was checked with Levene's test. The push-up test results and the total volume of the gray matter volume displayed a positive result in the homogeneity test of variances, so the between-group differences among the push-up test and gray matter volume was examined with the non-parametric Mann-Whitney U -test. For the analysis, all the fitness test results were made comparable between genders by diving each individual value with the mean result of the same gender. The volumetric variables were adjusted to the estimated total intracranial volume to remove the effect of the head size. Significance level of $p<0.05$ was used in all of the statistical calculations, and the effect sizes for Pearson's correlation were considered as small with $r > 0.1$, medium with $r > 0.3$ and large with $r > 0.5$.

3 RESULTS

3.1 Group statistics

The two groups, active and non-active, did not differ from each other in terms of age, puberty status, height, weight, or body mass index (BMI). Detailed information about the basic information of the groups is presented on table 1.

TABLE 1. Mean age, puberty status, height, weight and body mass index (BMI) of the groups.

	Active	**Non-active**
N	18 (10 females)	17 (13 females)
Age	14.0 (±0.75)	14.3 (±0.63)
Puberty status	3.2 (±0.88)	3.5 (±0.62)
Height (cm)	161.7 (±8.7)	164.9 (±8.6)
Weight (kg)	53.4 (±10.1)	54.5 (±8.6)
BMI	20.1 (±2.44)	20.5 (±2.07)

The ‘active’ group outperformed the ‘non-active’ in three of the five fitness tests (Table 2). A significant difference between the groups was noticed in the 20m line run test ($t(30) = 3.997$, $p<0.001$) (Figure 4), upper body lift test ($t(30) = 2.148$, $p<0.05$) and the push-up test ($p<0.01$, using a Mann-Whitney U -test) (Figure 6). Also the difference between 5 continuous jumps test was close to significant level ($t(30)=2.012$, $p=0.053$) (Figure 5). The throw-catch combination test did not show a significant difference between the groups ($t(30) = 1.488$, $p=0.15$) (Figure 7). Adjusted values (individual results divided by gender mean) for the active and non-active were 1.21 and 0.80 in the 20m line run test, 1.04 and 0.96 in the 5 continuous jumps test, 1.26 and 0.79 in the push-up test, 1.22 and 0.83 in the upper body lift test and 1.11 and 0.98 in the throw-catch combination test, respectively.

TABLE 2. Mean results of the groups from the fitness tests.

	Active	Non-active
20m line run	6.9 minutes***	4.2 minutes***
5 continuous jumps	9.6 meters	8.7 meters
Push-up (repetitions)	28.8**	19.8**
Upper body lift (repetitions)	49.2*	31.5*
Throw-catch combination	12.9 / 20 repetitions	11 / 20 repetitions

***p<0.001, **p<0.01, *p<0.05 significant difference between the groups

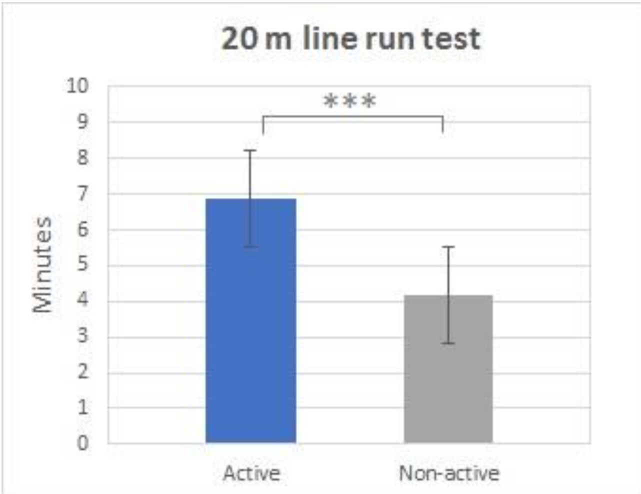

FIGURE 4. Mean results for the active and non-active groups in the 20 meter line run test, ***p<0.001 significant difference between the groups.

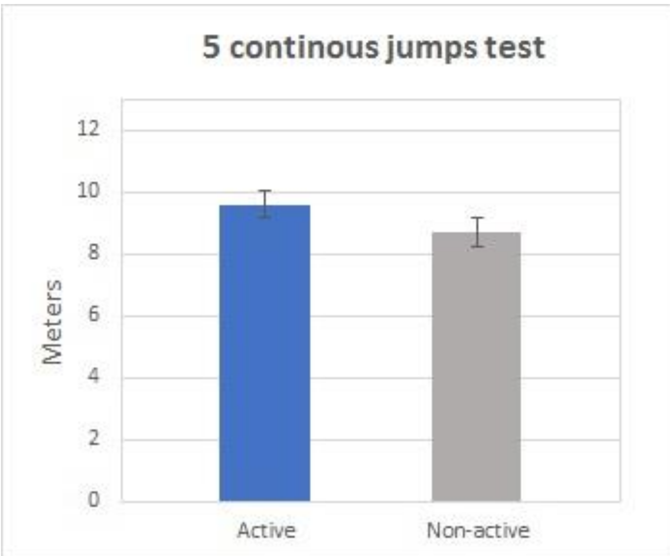

FIGURE 5. Mean results for the active and non-active groups in the 5 continuous jumps test, no significant difference between the groups (p=0.053).

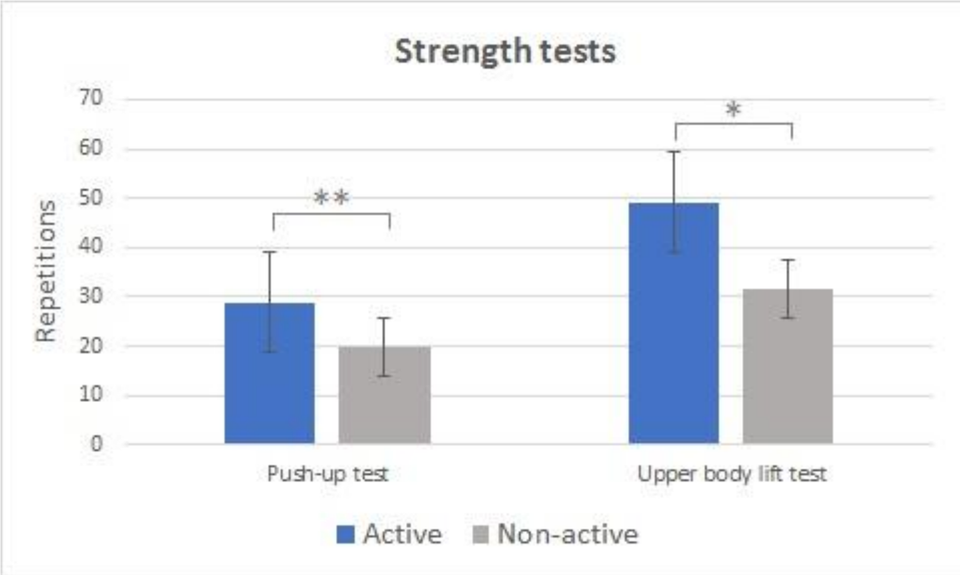

FIGURE 6. Mean results for the active and non-active groups in the push-up test and upper body lift test, **p<0.01 and *p<0.05 significant differences between the groups.

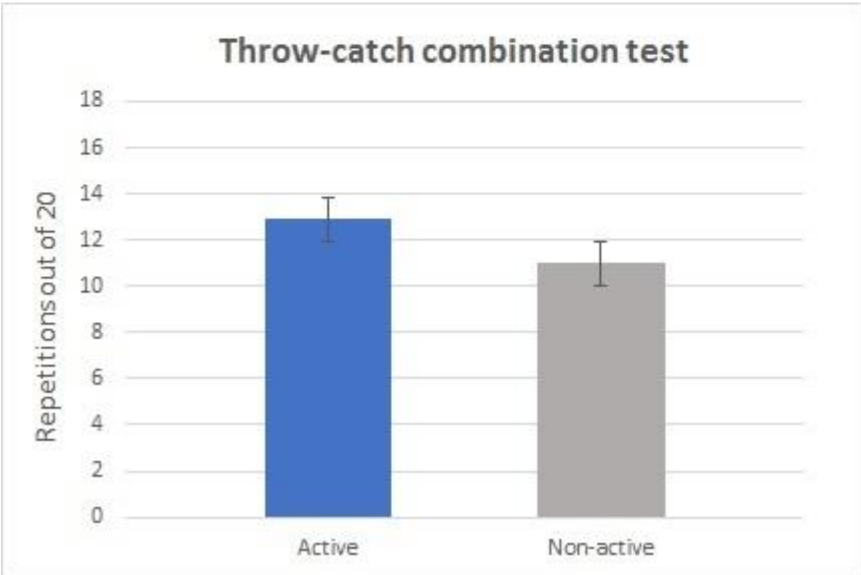

FIGURE 7. Mean results for the active and non-active groups in the throw-catch combination test, no significant difference between the groups (p=0.15).

3.2 Physical activity and brain morphology

There were no significant relationships observed between the level of physical activity and the volumetric variables inspected. No between-group differences were found in the total volume of the cortex, gray matter volume, white matter volume, or the hippocampal volumes (right and left). Detailed information is presented on table 2 below.

TABLE 2. Results for the volumetric variables.

Variable	Sig.	df	F	Partial Eta Squared
CortexVol	0.778	1, 30	0.081	0.003
GM[1]	0.443	-	-	-
WM	0.344	1, 30	0.923	0.030
Hippocampus (right)	0.595	1, 30	0.289	0.010
Hippocampus (left)	0.464	1, 30	0.550	0.018

Sig. = significance/p-value, df = degrees of freedom, F = F-test value, Partial Eta Squared (η^2) = measure of effect size, CortexVol = total volume of the cortex, GM= total gray matter volume, WM = total white matter volume

[1]*differences between GM was examined with a non-parametric Mann-Whitney U -test*

From the cortical thickness variables, the level of physical activity had a significant relationship with the thickness of the parahippocampal cortex of the right hemisphere. This relationship was positive; physically more active subjects expressed a thicker right parahippocampal cortex compared to less active subjects. A relationship between physical activity and the left paracentral cortex was also found, yet the significance of this connection was lost after controlling the effect of age. The relationship between physical activity and the left paracentral cortex thickness was positive, whereas age and the thickness of the left paracentral cortex displayed a negative relationship. No other significant relationships were observed, including the total thickness of the right and left hemispheres, precentral cortices, right paracentral cortex, postcentral cortices, superior frontal cortices and the parahippocampal cortex of the left hemisphere. Detailed information is presented on table 3 and figure 8 below.

TABLE 3. Results of the analysis of covariance (ANCOVA) for the thickness variables.

Variable	**Sig.**	**df**	**F**	**Partial Eta Squared**
Right hemisphere	0.450	1, 30	0.586	0.019
Left hermisphere	0.461	1, 30	0.557	0.018
Precenral (right)	0.665	1, 30	0.192	0.006
Precentral (left)	0.295	1, 30	1.136	0.036
Paracentral (right)	0.506	1, 30	0.453	0.015
Paracentral (left)	0.124	1, 30	2.500	0.077
Postcentral (right)	0.223	1, 30	1.549	0.049
Postcentral (left)	0.231	1, 30	1.494	0.047
Parahippocampus (right)	**0.044***	**1, 30**	**4.440**	**0.129**
Parahippocampus (left)	0.195	1, 30	1.757	0.055
Superior frontal (right)	0.875	1, 30	0.025	0.001
Superior frontal (left)	0.993	1, 30	0.000	0.000

*significance at the level of $p<0.05$

Sig. = significance/p-value, df = degrees of freedom, F = F-test value, Partial Eta Squared (η^2) = measure of effect size

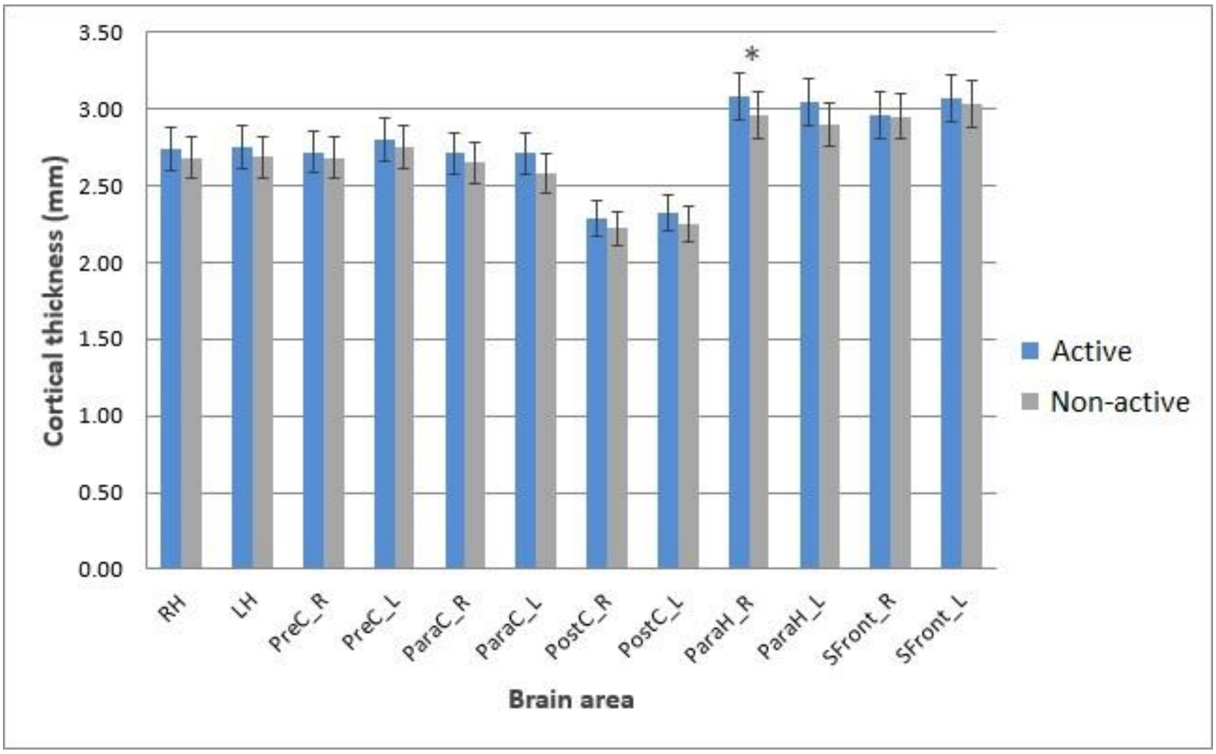

FIGURE 8. Mean cortical thickness in examined brain areas of the groups.

RH = Right hemisphere, LH = Left hemisphere, PreC_R = Right precentral cortex, PreC_L = Left paracentral cortex, ParaC_R = Right paracentral cortex, ParaC_L = Left paracentral cortex, PostC_R = Right postcentral cortex, PostC_L = Left postcentral cortex, ParaH_R = Right parahippocampal cortex, ParaH_L = Left parahippocampal cortex, SFront_R = Right superior frontal cortex, SFront_L = Left superior frontal cortex.

*significance at the level of $p<0.05$

3.3 Physical fitness and brain morphology

From the volumetric and cortical thickness variables examined, no brain area showed significant correlation with the physical fitness variables measured; the 20 meter line run test, the 5 continuous jumps, the strength tests (push-up & upper body lift) or the throw-catch combination test. However, despite not reaching the significance level, various fitness tests and brain areas showed correlation of small effect size ($r > 0.1$) in relation to each other, and some variables showed also correlation close to the medium effect size ($r > 0.25$). A positive, yet statistically non-significant, correlation close to the medium effect size was found between the throw-catch test and the hippocampal volumes (right: r=.296, p=1.00, left: r =.261, p=1.49), strength and the thickness of the left paracentral cortex (r=.266, p=0.141) and between strength and the thickness of the left superior frontal cortex (r=.271, p=1.34).

Negative, yet statistically non-significant, correlation close to the medium effect size was found between the 20m line run test and the total volume of the cortex (r=-.292, p= 0.105), 20m line run test and the total gray matter volume (r=-.253, p=0.163), 5 continuous jumps test and the thickness of the right precentral cortex (r=-.279, p=0.123), 5 continuous jumps test and the thicknesses of the postcentral cortices (right: r=-.289, p=0.108, left: r=-.260, p=0.151) and between the throw-catch test and the thickness of the right postcentral cortex (r=-.299, p=0.096). Correlations (Pearson's r) are presented on tables 4 and 5 below.

TABLE 4. Correlations between physical fitness tests and volumetric variables of the brain.

	20m run	**5-jump**	**Strength**	**Throw-catch**
CortexVol	-.292	-.233	-.046	-.128
GM	-.253	-.147	.003	-.056
WM	-.143	-.118	-.116	-.017
HC (right)	.002	.176	.120	.296
HC (left)	.097	.133	.077	.261

CortexVol = total volume of the cortex, GM = total gray matter volume, WM = total white matter volume, HC = volume of the hippocampus

TABLE 5. Correlations between physical fitness tests and cortical thickness variables.

	20m run	**5-jump**	**Strength**	**Throw-catch**
Right hemisphere	-.092	-.237	.031	.111
Left hemisphere	-.040	-.125	.122	.175
Precentral (right)	-.080	-.279	-.078	-.006
Precentral (left)	-.128	-.182	.019	.041
Paracentral (right)	-.027	-.044	.234	-.090
Paracentral (left)	.166	.043	.266	-.164
Postcentral (right)	-.164	-.289	-.055	-.299
Postcentral (left)	-.126	-.260	-.029	-.164
Parahippocampus (right)	.101	.163	.237	.235
Parahippocampus (left)	.079	-.089	.222	.136
Superior frontal (right)	-.235	-.229	-.037	.045
Superior frontal (left)	-.049	.086	.262	.236

4 DISCUSSION

The aim of this study was to examine, whether physical activity or physical fitness has a relationship with brain morphology in youth. Physical activity expressed a positive relationship with the thickness of the right parahippocampal cortex, after controlling the effect of age, puberty status and body mass index. Physically more active individuals had thicker right parahippocampal cortex, when compared to less active individuals. A positive relationship was also found between physical activity and the thickness of the left paracentral cortex, yet this finding was not significant after controlling the effect of age. Whereas physically more active individuals expressed a thicker left paracentral cortex compared to less active individuals, older subjects had thinner left paracentral cortex compared to younger subjects. These results add understanding to the associations between physically active lifestyle and brain morphology in youth.

4.1 Physical activity and brain morphology: the hippocampal area

A relationship between physical activity and the thickness of the right parahippocampal cortex (PHC) of the right hemisphere was found. Physically more active individuals seemed to have thicker right PHC compared to less active subjects. The hippocampal region and medial temporal lobe are essential for human cognition and memory (Shohamy et al., 2013). Adjacent to hippocampus, the parahippocampal cortex has been shown to have an important role especially in visuospatial processing and episodic memory. The parahippocampal area seems to respond strongly to visual scenes and it is thought to be involved in functions like spatial representation and navigation. These functions seem to be dependent on the posterior part of the PHC, hence the name 'parahippocampal place area' (PPA). In addition to the strong associations to scene stimuli, the PHC is involved in episodic memory, specifically in contextual associative processing. The PHC is therefore also important in binding different objects, places and relations into a single representation in memory. (Aminoff, Kveraga & Bar, 2013; Baumann & Mattingley, 2016). Since physical activity seems to have an effect on the anatomy of the parahippocampal cortex, it might also have an effect on PHC related cognitive functions, such as visuospatial and contextual processing.

Differences between brain volumes can be explained by various factors, including neurogenesis, synaptogenesis, myelination, angiogenesis or changes in axon or glia cell number and size (Zatorre et al., 2012). Here, the specific underlying cause for the greater cortical thickness in the active group remains unknown, yet a recent research by Bracht et al. (2016) showed, that physical activity in young healthy adults was linked to greater myelination of the right parahippocampal cortex. In other words, physical activity was connected to the white matter microstructure of the right PHC (Bracht et al., 2016). Myelination has been noticed to increase linearly up to age 20 (Houston et al., 2014), yet this evidence supports the idea, that physical activity might increase the process even further. With myelination, the neurons are covered with a fatty sheath, which enhances the efficiency of information transmission in brains (Houston et al., 2014). Although the current study cannot conclude the cause for the larger volume of the right parahippocampal cortex of the physically active individuals, higher myelination might be a plausible explanation.

Apart from the right parahippocampal cortex, no other brain area expressed a significant relationship with the level of physical activity, after controlling the effects of age, puberty status and BMI. Especially hippocampus has been linked to physical activity induced changes in several previous studies, although the findings have been mainly discovered with elderly (Hillman et al., 2008). However, a study by Rottensteiner et al. (2015) compared active and non-active young adults and found no differences in hippocampal volumes between the groups. It was suspected, that all the subjects' hippocampal-dependent memory functions were already at so high level, that exercise did not have an effect on hippocampus or the effect was so small it could not be detected. (Rottensteiner et al., 2015). A similar explanation might apply to the findings of the current study as well. The lack of discovered connections between physical activity and hippocampal volume might also be explained by the large-scale MRI data processing of the current study. Previous studies have shown the dentate gyrus of the hippocampus to be especially sensitive to physical activity induced changes and to display neurogenesis (Yau et al., 2014), yet the current study did not examine hippocampal subfields, which would have given more detailed information about brain morphology.

4.2 Physical activity and brain morphology: motor cortices and frontal brain regions

A relationship between physical activity and the left paracentral cortex was found, yet the result was not significant after controlling the effect of age. Whereas physical activity and the thickness of the left paracentral cortex had a positive relationship, age displayed a negative relationship with the thickness of the left paracentral cortex. In other words, physically more active individuals had thicker left paracentral cortex compared to less active subjects, whereas older subjects had thinner left paracentral cortex compared to younger subjects. Cortical thinning has been noticed to take place in almost all brain areas due aging, with the greatest changes occurring in adolescence (Tamnes et al., 2010). The decrease in cortical thickness can therefore be considered as a normal phase in brain development, yet the process might be influenced to some extent by external factors, such as physical activity. In addition, physical activity has been noticed to decrease during adolescence (Kokko et al., 2016), contributing also to the effect of age on brain morphology.

The primary somatomotor cortex is located in the central parts of the paracentral cortex, and the paracentral area has somatosensory representations of the foot and leg (Spasojević, Malobabic, Pilipović-Spasojević, Djukić-Macut & Maliković, 2013). Since the motor cortex is crucial for the execution of voluntary movement (Shenoy, Sahani & Churchland, 2013), it is quite logical for physical activity to express a relationship with the area. Although higher level of physical activity seemed to predict thicker left paracentral cortex, the connection was overpowered by the effect of age. Whereas the adolescent brain seems to express cortical thinning to a great extent (Tamnes et al., 2010), it would be interesting to assess the connection between physical activity and the thickness of the paracentral cortex in adults, whose brains have reached a more stable developmental phase and might therefore express the changes induced by external influences more clearly. In addition, further research should assess the relationship between physical activity and cortical thickness in a longitudinal study. For example, Schnack et al. (2015) established that intelligence was in fact connected to the change in cortical thickness, rather than with thickness itself. They concluded, that faster thinning of the left cortex was connected to higher intelligence in children, whereas after the age of 21, the reverse was true. These findings suggest, that thicker cortex might be either positive or negative, depending on the developmental phase of the brain. In the current study, physically more active individuals seemed to express a trend of thicker cortex among all the examined brain areas compared to less active ones, although only one area reached a significant difference. It seems, that the thickness of the cortex is a highly equivocal variable, especially in youth, when developmental changes are occurring simultaneously with possible changes caused by external factors. Therefore, further research would be necessary to examine the behavioral and cognitive consequences the cortical thickness reflects.

In contrast with previous findings, physical activity did not express a relationship with the frontal brain regions. Physical activity and exercise have been previously linked with increased gray matter volume and changes in activation of the frontal regions (Hötting & Röder, 2013). However, in the current study, the focus was only on the structure of the brain. Therefore, nothing can be said about the activation patterns of frontal regions and the possible differences between the active and non-active subjects. In addition, previous studies have shown physical activity to benefit especially executive functions dependent from the frontal regions (Guiney & Machado, 2013). However, differences in cognitive functions are not necessarily expressed in the structural level, which might also explain the lack of observed connections between physical activity and the frontal regions in the current study. In addition, the only frontal area examined in the current study was the thickness of the superior frontal cortex. For more precise results, also the MRI data processing would have required more precision.

4.3 Aerobic fitness and brain morphology

The active group outperformed the non-active group in four of the five fitness tests, with the biggest difference established in the 20m line run test. This implies that physically active lifestyle is strongly connected to higher level of aerobic fitness. However, no significant relationships were found between aerobic fitness and brain morphology, although there was a relationship between physical activity and cortical thickness in specific regions. This indicates that physical activity does not necessarily have to improve physical fitness to influence brain morphology in youth.

In line with the previous finding by Herting and Nagel (2013), aerobic fitness was not related to either total gray or total white matter volume. This reinforces the suggestion that aerobic fitness has an influence on specific brain areas, which are not expressed in larger scales. However, in contrast to previous studies, aerobic fitness did not show connections to any specific brain areas either, including the hippocampal area and the frontal brain regions. Aerobic exercise and improved cardiovascular fitness have been noticed to increase the volume of the hippocampus in both adolescents and older adults (Erickson et al., 2011; Herting & Nagel, 2013), yet this could not be represented in the current study. This reinforces the assumption, that physical activity does not necessarily have to increase aerobic fitness to cause changes in brain morphology. In their review about the benefits of physical exercise on cognition, Hötting and Röder (2013) conclude that cardiovascular fitness explains only a fraction of the variation in the cognitive variables, which might reflect the changes in the brain morphology as well.

Although previous studies have suggested a relationship with aerobic fitness and the frontal brain regions (Chaddock et al., 2012; Colcombe et al., 2006), this could not be represented in the current study. Possible reasons for this might include the age of the subjects or the undetailed processing of the MRI data. The connections between aerobic fitness and frontal brain regions have been previously established with either children (Chaddock et al., 2012) or older participants (Colcombe et al., 2006), suggesting that adolescents and young adults might not express similar benefits due to higher fitness as in childhood or with aging. The adolescent brain might also express such great anatomical and functional changes, that the possible effects of external influences, such as physical activity or fitness, cannot be observed. In addition, the current study looked at only one area of the frontal brain regions without more precise examination. Finally, the current study cannot conclude, whether the frontal lobe mediated cognitive functions would have been better in the active group, since only the anatomical between-group differences were examined. Several previous studies have found a better performance in executive tasks in highly active or more fit subjects (Guiney & Machado, 2013), yet here the focus was merely in the morphology of the brain.

Williams et al. (2016) discovered that higher peak VO2, an estimate of aerobic fitness, was connected to thinner cortex in young adults. In addition, a study by Chaddock-Heyman et al. (2015) found decreased gray matter thickness in superior frontal cortex in higher-fit children. Whereas larger brain volumes have often been connected with higher intelligence, it has been suggested, that the relationship might be reversed in youth. In their extensive study, Schnack et al. (2015) discovered that faster cortical thinning of the left cortex was connected to higher intelligence in adolescents. The correlation between aerobic fitness and the total volume of the cortex, as well as the correlation between aerobic fitness and total gray matter volume were slightly negative also in the current study, yet these findings did not reach significance. It is however possible, that individual differences in aerobic fitness can affect some brain areas showing considerable changes in cortical thickness during development, leading to positive changes in cognitive processing and intelligence (Chaddock-Heyman et al., 2015; Schnack et al., 2015).

4.4 Strength, motor skills and brain morphology

The active group outperformed the non-active also in the strength tests, linking physical activity to better muscular endurance as well. Also the five continuous jumps test, measuring power production of lower limbs, was close to expressing a significant difference. No between-group difference was found in the throw-catch combination test. This implies that perceptual motor skills and handling skills are independent from the level of physical activity.

Although no significant correlations were found between the physical fitness tests and brain variables, there were several variables showing correlation close to moderate effect size. The throw-catch combination test, measuring handling and perceptual motor skills, displayed a slight positive, yet non-significant, correlation with the volumes of both right and left hippocampus. Animal studies have suggested, that physical skill training can increase the number of newly-born neurons in the hippocampus in both adolescents and adults (Curlick et al., 2013; DiFeo & Shors, 2017). Although results from animal studies should always be implied to humans with extreme caution, they might however offer plausible explanations that would otherwise be impossible to confirm in humans. Even though the correlation between motor skills and hippocampal volume established here was only moderate and did not reach significance, it can still be regarded as a possibility that better performance in a motor skill task is connected to either increased neurogenesis or survival of the newly-born neurons, therefore leading to a larger hippocampal volume.

A modest non-significant positive correlation was also found between strength and the thickness of the left paracentral cortex. The thickness of the left paracentral cortex displayed a correlation also with the level of physical activity, making it an interesting brain area for further research considering the effects of both physical activity and fitness. Previous studies have found a link between grip strength and motor cortex volume, as well as with white matter volume (Kilgour et al., 2014; Koppelmans et al., 2015). However, the strength tests in the current study did not measure maximal strength, and further research would be necessary to examine, whether muscular endurance could have similar influences on brain morphology.

Slight negative, yet non-significant, connections were found between the fitness test variables and the motor cortex regions, especially the right precentral cortex and the postcentral cortices. Contrary to the results from previous studies, also the throw-catch combination test result showed a slight negative non-significant connection with the thickness of the right postcentral cortex, although previous studies have discovered rather larger volumes in the motor cortex areas (Gryga et al., 2012; Sampaio-Bapista et al., 2014). These findings might, however, reflect merely the normally occurring cortical thinning in the adolescent brains (Tamnes et al., 2010).

4.5 Strengths and limitations of the study

Previous studies examining the relationship of physical activity and fitness to brain morphology have been mostly animal studies (Yau et al., 2014), whereas this study offered additional information on the topic using human subjects. In addition, the study was conducted with less examined population, the youth. An objective measurement of physical activity was used instead of less reliable self-evaluation questionnaires and also the brain imaging was performed on a high-technology equipment, providing high-quality MRI data. Both of these add reliability to the acquired results of the study.

Limitations of the study include a modest number of subjects, the cross-sectional nature of the study and possible inaccuracies in the physical activity and fitness measurements. With a larger study sample, the results could be generalized with higher reliability. However, including both males and females in the age range of 12 to 15 years, the results can be reliably generalized to other healthy Finnish adolescents of that age group. Being a cross-sectional study, the cause or consequence cannot be implied from the results. However, previous studies have already suggested that brain morphology could be altered with physical activity and exercise (Colcombe et al., 2006; Erickson et al., 2011), so the level of activity can be cautiously assumed to be the cause in the findings of this study as well. Possible inaccuracies in the physical activity and fitness measurements should also be taken into account. For example, measured physical activity from the sample week is merely assumed to represent a normal pattern of behavior, and there are also some technical limitations concerning the hip-worn accelerometers. Activities, where the hip stays in one vertical plane (i.e. cycling) or where the hip stays relatively still despite of heavy loading on muscles (i.e. resistance training), are often underestimated in how vigorous the activity is (Ainsworth et al., 2015; Hansen et al., 2014). In addition, the physical fitness measurements used in the current study were field tests instead of highly standardized, objective laboratory tests. Possible inaccuracies concerning the fitness tests results might be due to varying movement standards, lack of motivation or simply errors in counting the repetitions or measuring the results. The differences in the test protocols among girls and boys is also an issue to be considered, even though the results were adjusted to eliminate the gender differences. Finally, although the effect of age, BMI and puberty status was controlled, there might have been other variables to interfere with the relationship of physical activity and brain anatomy that were left out of the analysis.

4.6 Conclusions

The current study was one of the first to link physical activity and fitness specifically to brain variables in youth, and thus offered additional information about the relationship of physically active lifestyle and brain morphology in youth. The aim of this study was to examine, whether physical activity or fitness has a relationship with regional brain volume or cortical thickness in youth. Hypothesis based on previous studies was, that physically more active and fit adolescents would express differences in brain morphology compared to non-active and less-fit adolescents, expectedly in the areas of hippocampus, frontal brain regions and/or motor cortex. In line with our hypothesis, a relationship between the level of physical activity and the thickness of the right parahippocampal cortex was established. Physically more active individuals had thicker right parahippocampal cortex compared to less active individuals. A relationship between physical activity and the thickness of the left paracentral cortex, a part of the motor cortex, was also found, although this finding lost significance after controlling the effect of age. Whereas physically more active individuals had thicker left paracentral cortex compared to less active individuals, older subjects had thinner left paracentral cortex compared to younger subjects. However, in contrast to our hypothesis, no significant connections were found between the level of physical fitness and regional brain volume or cortical thickness.

These findings imply that the area of right parahippocampal cortex might be especially prone to physical activity induced changes in youth, and that physical activity does not necessarily have to improve physical fitness to cause changes in brain morphology in youth. Additional further research could examine, whether physically active lifestyle in youth can enhance also parahippocampal mediated cognitive functions, such as visuospatial and contextual processing. In addition, further research should focus on longitudinal studies on the topic, since the brain morphology changes might reflect different causes depending on the developmental phase of the brain.

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