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Physical exercise and cortical thickness in healthy controls: a pilot study

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Abstract. – OBJECTIVE: Physical exercise has showed potential in improving brain function and increase in cortical size. This study aims to assess the cortical changes that are associated with physical exercise.

SUBJECTS AND METHODS: We investigated 45 subjects; 25 of them involved in exercise group and 20 in non-exercise group. The exercise group underwent 6 months of intervention consisting of 40 minutes (min) of aerobic exercise and 20 minutes of anaerobic exercise. Magnetic resonance imaging (MRI) scans were acquired from both groups to measure the thickness of the cortex and was assessed with FreeSurfer software.

RESULTS: Exercise group demonstrated significantly increased cortical thickness in the left pericalcarine area, left superior parietal area, right rostral middle frontal and right lateral occipital gyrus compared to non-exercise group.

CONCLUSIONS: Regular and continuous physical exercise can enhance brain structures. The current findings have important implications for understanding the effect of physical activity or fitness programs on the brains of healthy individuals and of patients with a range of conditions.

Key Words:
Physical exercise, Cortical thickness, Connectivity.

Introduction

The cerebral cortex is the outer layer of gray matter covering both hemispheres. It contains more than 10 billion neuronal bodies, with thickness varies from 1.5 to 4.5 mm. The mean distance from the grey-white matter boundary to the grey-cerebrospinal fluid boundary within a defined cortical region is how to measure cortical thickness size[1]. In recent years, studies[2-4] have been performed using non-invasive brain imaging techniques to investigate exercise-related changes in structural and functional modifications in the brain, influence cognitive functions, and provide psychological and biological benefits. These studies[2-4] provide compelling evidence that exercise has a positive effect on brain structure.

A study[5] done in 2020 about the effect of aerobic exercise on cortical thickness in patients with schizophrenia showed that after 12-week of intervention, an increase in the cortical thickness of the right entorhinal cortex and an associated improvement in social adaptation. In 2017, aerobic exercise intervention study showed cognitive performance, and brain structure reported that the aerobic group showed an increase in the cortical thickness of dorsolateral prefrontal cortex compared to baseline, but with no changes in cortical thickness of ventrolateral prefrontal cortex or hippocampus[6].

Furthermore, a study[7] on aerobic fitness in cortical thickness and mathematics achievement in preadolescent children divided into higher fit and lower fit groups showed decrease in cortical thickness in the higher fit children in superior frontal, temporal, and lateral occipital. The aer-

Corresponding Author: Shahid Bashir, MD; e-mail: sbashir10@gmail.com obic fitness groups were not associated with any gray matter thickness differences in brain areas, like the middle frontal, middle temporal[7]. A randomized control trial about the effect of aerobic exercise on cognition in younger adults showed a significant improvement in executive function in the aerobic exercise group. It significantly increased cortical thickness in the left caudal middle frontal cortex Brodmann area with no age exercise connection[8].

Physical exercise is well-known to have effects on brain health and cognitive performance. There are different mechanisms to which exercise can affect the brain, like increased blood flow through vascularization and induction of neurotrophic factors[9]. However, few studies discuss the connection between physical exercise and cortical thickness.

To the best of our knowledge, few studies have been conducted, and more effort is needed to explore these cortical changes. This study aims to investigate the effects of physical exercise on cortical thickness in healthy individuals.

Subjects and Methods

A total of 45 subjects, divided into the exercise group (n=25) and the non-exercise group (n=20), were included in the study. Participants were between 19 and 27 years of age; the groups matched for age, and all were males. All included individuals were physically healthy, meaning that they showed no evidence of significant cardiovascular, neuromuscular, musculoskeletal, endocrine, or other somatic disorders. None of the participants had a primary diagnosis of alcohol or substance abuse or dependence. All participants in the control group were physically inactive, defined as engaging in less than one hour of moderate physical activity weekly.

The Institutional Review Board approved the study at King Saud University (IRB-KSU-E-13-983). Informed written consents were obtained from all participants.

Exercise Group

All participants were healthy with no history of physical or mental illness. All subjects underwent a six-month intervention consisting of physical exercises (PE). Participants in the exercise group engaged in 1 h of PE daily, consisting of 40 min of aerobic exercise and 20 min of anaerobic exercise. Aerobic exercise was performed using an upright bicycle ergometer (2 min of warm-up, 4 min of cycling with tolerable workload, 2 min of cool down for stretching and breathing), a recumbent bicycle ergometer (warm up at a comfortable pace with low resistance for 2 min, then, working harder by increasing the resistance as tolerable for 4 min, and finally, pace back by decreasing the resistance to a comfortable level for cooling down for 2 min), a rowing machine (warm up at a low intensity for 2 min with the aim for 15-20 strokes per min (SPM), followed by increasing the resistance and exertion with the aim for reaching 25-35 SPM for 4 min, then cool down at a low intensity for 2 min), a cross trainer (warm up at a low intensity for 2 min with the aim for 40-50 stride per min, followed by increasing the resistance with the aim for 60-80 stride per min for 4 min, then cool down at a low intensity for 2 min) and a treadmill (warm up by walking for 2 min, then easy run at tolerable speed for 4min and finally cool down by walking for 2 min). The anaerobic exercise consisted of weight training (6 exercises per week, 3 sets, 10-15 repetitions; exercises engaged the biceps, triceps, abdominal muscles, quadriceps, pectoral muscles, and deltoid muscles).

Non-Exercise Group

All participants in the control group were physically inactive, defined as engaging in less than one hour of moderate-intensity aerobic physical exercise or vigorous-intensity aerobic physical exercise; or an equivalent combination of both types throughout the week[9].

Brain Imaging

Brain scans were acquired on Siemens Magnetom Verio 3T MRI clinical scanner (Siemens AG, Healthcare Sector, Erlangen, Germany) at KSU Medical City Riyadh, Saudi Arbia. 12-channel phased-array head coil were used to acquire: T1-weighted 3D magnetization-prepared rapid gradient-echo imaging (MPRAGE): TR = 1600 ms, TE = 2.19 ms, inversion time = 900 ms, flip angle = 9°, acquisition plane = sagittal, voxel size = $1 \times 1 \times 1$ mm^3, FOV = 256 mm, acquired matrix = 256×256, acceleration factor (iPAT) = 2.

Post-Processing

FreeSurfer software (Martinos Center for Biomedical Imaging, Charlestown, MA, USA) was used for cortical thickness measurement of the whole brain. FreeSurfer is a semi-automated brain morphometry tool. The details of this post-processing sequence have been described elsewhere[10-13]. Briefly, the processing stream includes a Talairach transform of each subject's native brain, segmentation of the gray/white matter boundaries. Cortical thickness measurements were then obtained by calculating the distance between these two boundaries across the entire cortical mantle of each hemisphere[11]. The global mean cortical thickness for each subject was computed by averaging the cortical thickness at each vertex and was used in the statistical analysis. The cortical map of each subject was smoothed with a Gaussian kernel of 15 mm full width at half-maximum for the entire cortex analyses.

Statistical Analysis

By using FreeSurfer software, all statistical tests were performed with critical P-value for significance set at <.05 with correction for multiple comparisons. In case when there were no significant voxels, we performed a separate analysis with p-value for significance set at < .001 without correction of multiple comparisons (uncorrected). The general linear model (GLM) was implemented at each vertex in the whole brain to identify the brain regions where the exercise groups showed significant cortical thickness relative to controls with age as nuisance variable.

Results

The exercise group demonstrated significantly increased cortical thickness in the left pericalcarine area, left superior parietal area, right rostral middle frontal, and right lateral occipital gyrus. In controls, there was increased cortical thickness in the bilateral precuneus, anterior cingulate, middle temporal, lateral orbitofrontal, supramarginal gyri and left fusiform, left inferior temporal, left superior parietal gyrus, right pars opercularis, and right medial orbitofrontal cortex (Figure 1).

Discussion

Our result in the exercise group had a direct effect of the intervention on cortical thickness in the left pericalcarine area, left the superior parietal area, right rostral middle frontal, and right lateral occipital gyrus. The cerebral cortex is a thin sheet composed of neurons and glial cells, which vary in thickness between brain regions. The variability of thickness reflects the total neuronal body count, cell type, and packing in that region. The diversity of cortical thickness in the human brain occurs early in development and develops asymmetrically into adulthood and old age[14].

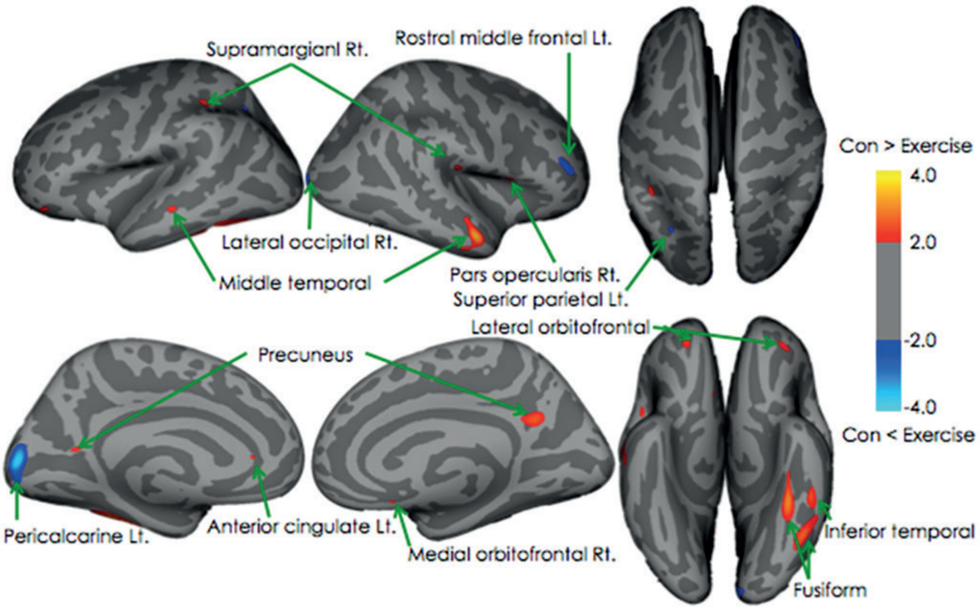

Figure 1. Statistical maps showing increased cortical thickness in the exercise group (*blue*) and in the control group (*red*) (p<0.001 uncorrected).

One study[7] showed that subjects who were higher fit and doing exercises had decreased lateral occipital thickness and no change in middle frontal and superior parietal areas compared to our study, which showed an increase in these areas. While another randomized control trial[8] was done for six months showed that the aerobic exercise group had only an increase in left caudal middle frontal area in the Brodmann area and with no change in other regions. Likewise, a trial[6] reported an increase in the cortical thickness with aerobic exercise in only the dorsolateral prefrontal cortex compared to baseline, which was not found in our study. Another region that has been reported positively affected by physical exercise over 12 weeks in both mild cognitive impairment and healthy elders is the parietal cortical area which is consistent with our data[15]. Furthermore, the study showed an increase in other regions associated usually with Alzheimer's disease atrophy pattern bilateral inferior frontal gyri, insula, left medial temporal gyrus, posterior cingulate, and the right medial superior frontal gyrus and precuneus, which were increased in the control group[15].

Our result supports the existing research that physical exercise affects the cortical surface. The effect did not differ by age. Thus, our findings suggest exercise may improve brain health and function through cortical thickness. The current literature has repeatedly reported that different areas of the cortex are affected by exercise, suggesting that some underlying factors control which areas of the cortex will be affected; thus, further research is needed to explore such differences.

The study has several limitations, which must be considered when interpreting the presented findings. Our study population compared to literature was relatively small. Furthermore, the training duration of the intervention is short compared to some other studies, in which interventions were carried for up to 2 years[16]. The most common exercise period in the literature is 6-12 months[17-19].

Conclusions

The current findings showed that regular aerobic exercise could boost the cortical thickness of different brain regions that are associated with memory and learning processing[20]. There is evidence[21] from randomized controlled trials that engagement in physical activity might enhance brain structure and function in terms of white matter integrity and activation of critical regions in cognitive processes. Likewise, review research[22] of multiple brain imaging studies indicates that regular aerobic exercise increases gray matter volume in at least eighty percent of the brain. All together suggest that regular physical exercise can be prescribed as prevention and treatment to counter the shrinking of the brain regions, such as the hippocampus, and protect against expected memory impairment and cognitive decline of normal aging[23,24]. There is clear evidence[25,26] of physical exercise treatment efficacy for different psychiatric, and neurological disorders. However, it is worth mentioning that different studies showed an increase in different brain areas, which may suggest that other factors can influence which part of the cortex improves. Continuous and regular exercise improves cortical thickness in the brain. The current findings have important implications for understanding the effect of physical activity or fitness programs on the brains of healthy individuals and patients with a range of conditions.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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