Cortical and Subcortical Brain Volume Alterations Following Endurance Running at 38.6 km and 119.2 km in Male Athletes

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: Although several studies have shown that ultramarathon running causes severe physical and mental stress and harms organ systems, its effect on brain tissue remains unclear. The purpose of this study was to investigate the volumetric change of cortical and subcortical brain structures following 38.6-km and 119.8-km mountain races.

Material/Methods: A total of 23 healthy male runners (age, 49.05±5.99 years) were classified as short-trail (ST; n=9) and ultra-trail (UT; n=14) endurance running. Pre- and post-test scanning of brain tissue was performed by using a 3-Tesla magnetic resonance imaging (MRI). Pre- and post-race differences in cortical and subcortical volumes in the ST and UT groups were separately determined by Wilcoxon signed-rank test.

Results: Cortical gray matter (GM) and cerebral GM volume significantly increased after the race in both ST and UT groups, whereas the volume of the thalamus, caudate, pallidus, and hippocampus significantly increased only in the UT group. Cerebrospinal fluid (CSF) and white-matter (WM) volumes did not change after endurance running and remained unaltered in both groups.

Conclusions: Endurance running has a site-specific acute effect on cortical and subcortical structures and may attenuate GM volume decrease in older adult male athletes. The increased volume of subcortical structures might be a response of physical exercise and additional physical stress experienced by ultramarathon runners.

Keywords: Diffusion Magnetic Resonance Imaging • Neuroimaging • Running

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Background

The beneficial effects of regular physical exercise on human health and quality of life have been widely accepted and documented, with relevant evidence that it significantly improves inactivity-related diseases such as hypertension, obesity, dyslipidemia, and cardiovascular disease [1-3]. Studies have proven that strenuous exercise performed over a certain intensity or workload harms the health and is associated with serious damage in many organs and systems [4,5]. Short-term endurance exercise has been reported to have severe adverse effects on the cardiorespiratory system [6], hormonal status [7], immune function [8], electrolyte metabolism [9], and muscle damage [10].

Running is one of the world's most popular sports performed for health, fitness benefits, enjoyment, and socialization [11]. Therefore, it is performed by millions of enthusiasts at various distances, even despite their advancing age [12,13]. Amateur runners start their running experience with short distances that may gradually increase up to ultramarathons, which are races longer than the traditional 42.2 km marathon. Ultramarathon races are performed at various distances, ranging from 50 km [14] up to continental races, but the most preferred distance seems to be over 100 km [15-17].

Most recreational ultramarathon runners reach their peak performance in their 40s and are willing to push their limits in extreme conditions that make them prone to diverse medical complications that vary from mild blisters and stress fractures to severe cardiac arrest or stroke [18-21]. Cardiac arrest [22], hyponatremia [23,24], increased arterial stiffness [25], and kidney dysfunction [26] were reported after ultramarathons, but the effect of physical overexertion on the brain remains unclear.

Recent studies clearly show the beneficial effects of moderate exercise on brain tissue, demonstrating that it can prevent and even reverse age-dependent decline in brain tissue and thereby improve cognitive functions of elderly people with dementia [27-29]. Thus, brain atrophy in the elderly can be prevented or slowed by aerobic exercise as a result of enhanced synaptic plasticity in the hippocampus and increased cell poliferation [30]. Moreover, increased blood flow to the hippocampus in adults is known to improve memory functions and increase neurogenesis [31]. Wood et al [32] reported increased cortical GM volume as a long-term adaptation to ultramarathon running in athletes with running experience of over 30 years.

To date, few studies have focused on the effects of ultramarathon running on the brain, and only 2 studies have focused on acute effects on cerebral volumetric changes during endurance running. The first prospective MRI study reported GM volume decline after a 4487-km multistage continental ultramarathon race [33]. On the other hand, Herm et al [34] found that WM volume was not altered after marathon running when compared to controls, and concluded that endurance running did not cause brain injury. However, results of these MRI studies are not comparable due to use of different measurement techniques and the nature and distance of the ultramarathon. Thus, more detailed research is needed to understand the effect and mechanism of ultramarathon running on brain tissue.

The purpose of this study was to identify the acute effects of marathon and ultramarathon running on cortical and subcortical structures in male runners by using a high-resolution 3-Tesla MRI.

Material and Methods

Participants

All runners signed an informed consent form before participation. The study adhered to the Helsinki Declaration, and Clinical Research Ethics Committee approval was obtained from the local university to eliminate ethical concerns (approval no. 83/09-10-2019). The quasi-experimental study was performed with nonrandomized groups and a pre- and post-test design.

Runners who enrolled to participate in the Salomon Cappadocia Ultra-trail 2019 event were contacted a few weeks before the race and requested to participate in the research. Enrollment criteria included either having a valid medical report stating that there was no health hazard for the person to participate in an ultramarathon run or having a permit approved by any sports federation. A total of 27 healthy amateur male runners (age, 49.05±5.99 years) were eligible for inclusion (age, handedness, health status), and were non-randomly grouped as short-trail (ST; n=12) or ultra-trail (UT; n=15) according to their registration preference for the race. We excluded participants who consumed alcohol or tobacco, had any kind of neurologic, psychologic, or metabolic diseases, or who had a history of traumatic brain injury.

Design

The measurements were performed 1 day before the race and immediately after the race. The Salomon Cappadocia Ultra-trail race is monitored by the International Trail Race Association (ITRA), and guarantees certain standards. Athletes were allowed to consume food, water, and hypotonic drinks at check points that had to be reached within certain time limits. ST and UT routes are given in detail in **Figures 1 and 2**, respectively.

The total altitude changes for the 38.6 km ST and 119.8 km UT races were 1120 m and 3730 m, respectively. Average temperature (day=16.5±3.1°C; night=8.8±2.1°C; 6-21°C), humidity

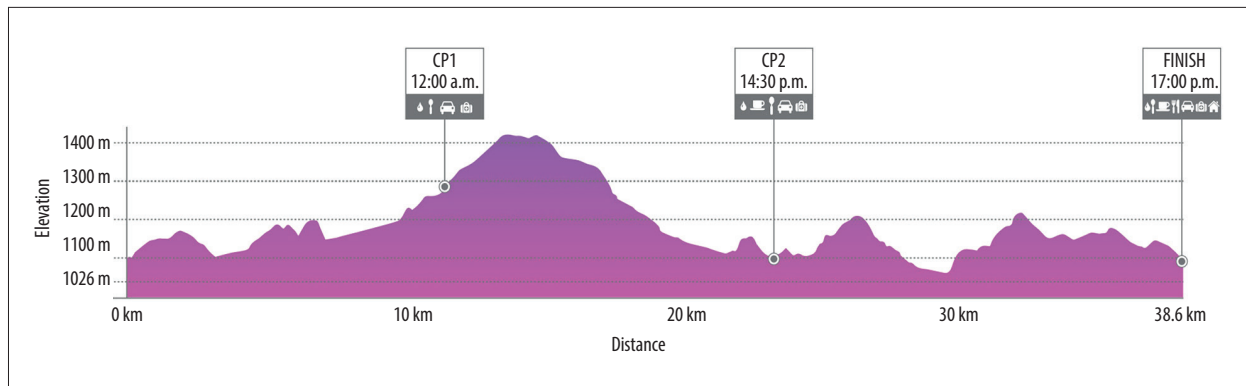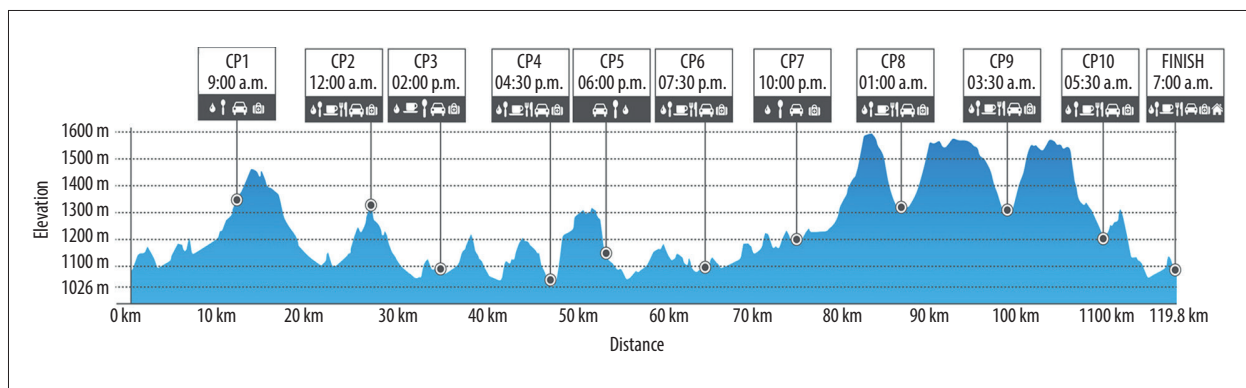**Figure 1.** Schematic representation of 38.6-km short-trail with detailed distance, altimetry, time zone, and check points (CP) (https://cappadociaultratrail.com).

Figure 2. Schematic representation of 119.8-km ultra-trail with detailed distance, altimetry, time zone, and check points (CP) (https://cappadociaultratrail.com).

(50±1.41%), and wind speed (13 km/h) were checked from AccuWeather (AccuWeather Superior Accuracy™), the Wet Bulb Globe Temperature index was calculated as 12.2°C, and the heat index was 17.23°C.

Materials and Procedures

Demographic and anthropometric data

Demographic data were obtained via questionnaire during pretest assessment, including personal information, medical conditions, and training history. Height, body weight, and body-mass index (BMI) of the athletes were assessed according to the standardized anthropometric procedures [35].

MRI Acquisition

Two brain scans were performed for each athlete by the same radiologist, 1 day before and immediately after the race. The time of the pre-race MRI scan of each athlete was planned according to the estimated time of arrival, which was calculated based on the athlete's prior race performance. Brain scans were obtained using a Siemens 3.0 Tesla MRI (Magnetom

Skyra, Siemens Healthcare, Erlangen, Germany) at the National Research and Education City Hospital. The 3D sagittal magnetization-prepared rapid-acquisition gradient-echo (MPRAGE) sequence (sagittal, repetition time (TR)=2300 ms, echo time (TE)=3.4 ms, field of view (FOV)=250 mm^2, matrix: 256×256, flip angle 7°, slice thickness=1 mm) of T1-weighted images was obtained in supine position.

MRI Processing

VolBrain (http://volbrain.upv.es) cloud-computing software was used for processing T1-weighted MR images. Cerebrospinal fluid (CSF), brainstem, gray-matter (GM), white-matter (WM), and total brain volumes of cortical and GM of subcortical structures, including thalamus, caudate, globus pallidus, hippocampus, accumbens, putamen, and amygdala were demonstrated as mean±SD (min–max). Prerequisite steps of the pipeline are explained in detail elsewhere [36].

Statistical Analysis

Whether the data showed normal distribution was tested by using the Shapiro-Wilk test by using the IBM statistical package

Table 1. Descriptive characteristics of runners in ST and UT groups.

Variables	ST (n=9) Mean±SD (Min–Max)		UT (n=14) Mean±SD (Min–Max)	
Age (years)	47.44±5.85	(40-58)	50.08±6.07	(40-60)
Height (m)	1.76±0.09	(1.65-1.87)	1.75±0.54	(1.65-1.83)
Weight (kg)	75.55±9.54	(61-91)	73.0±8.52	(60-91)
BMI (kg/m^2)	23.86±7.76	(21.74-26.67)	23.51±2.02	(22.01-28.41)
Running history (years)	6.66±7.46	(2-25)	9.64±5.66	(4-20)
Annual running distance (km)	2922.22±1170.23	(1500-4800)	4020±1600.78	(1100-6800)
Weekly running distance (km)	70.55±23.04	(30-110)	136.43±79.48	(50-350)
Weekly training volume (hours)	6.55±2.01	(4-9)	12.46±4.83	(7-22)
Average training speed (km/h)	5.54±0.63	(4.30-6.20)	5.16±0.60	(4.30-6.04)
Average race speed (km/h)	6.04±1.46	(4.18-7.54)	6.10±1.30	(5.10-8.98)

ST – short trail; UT – ultratrail; BMI – body mass index.

Table 2. Differences in volume of cortical and subcortical structures before and after 38.6 km race in short-trail group.

Volume (cm^3)	Prerace (n=9) Mean±SD (Min–Max)		Postrace (n=9) Mean±Sd (Min–Max)		Z	p
Brain total	1252.70±57.98	(1182.5-1319.73)	1287.07±55.13	(1204.15-1358.63)	-1.362	0.173
CSF	268.41±75.12	(165.35-379.57)	248.14±73.66	(148.66-372.86)	1.599	0.110
WM total	538.03±38.68	(479.28-598.37)	548.95±36.10	(484.24-592.32)	-0.889	0.374
GM total	714.67±34.64	(663.14-756.92)	738.12±33.75	(690.60-807.87)	-2.310	0.021*
Brainstem	26.87±1.85	(24.08-29.57)	27.26±2.05	(24.37-29.91)	-1.507	0.132
Cerebrum total	1074.81±59.75	(1003.05-1146.76)	1110.88±58.38	(1037.74-1189.61)	-1.718	0.086
Cerebrum WM	477.64±37.35	(424.06-537.76)	488.92±35.20	(429.38-533.32)	-1.481	0.139
Cerebrum GM	597.17±33.82	(546.62-638.35)	621.92±34.99	(571.20-690.21)	-2.310	0.021*
Cerebellum	151.03±10.10	(141-173.60)	148.98±10.71	(138.85-173.41)	0.652	0.515
Thalamus	11.79±1.43	(9.5-13.81)	12.336±1.07	(9.85-13.62)	-1.601	0.109
Caudate	7.68±0.83	(5.85-8.57)	7.67±1.02	(6.08-9.18)	0.949	0.342
Putamen	8.86±0.92	(7.73-10.40)	9.06±0.97	(7.94-10.76)	-1.543	0.123
Pallidus	2.61±0.15	(2.35-2.81)	2.69±0.18	(2.34-2.87)	-1.122	0.262
Hippocampus	8.89±0.76	(7.77-9.92)	8.95±0.61	(7.82-9.69)	-0.059	0.953
Amigdala	1.93±0.22	(1.67-2.29)	1.95±0.26	(1.54-2.28)	-0.178	0.859
Accubens	0.65±0.17	(0.38-0.85)	0.68±0.14	(0.43-0.89)	-0.535	0.593

* Significant differences at p<0.05. CSF – cerebrospinal fluid; GM – gray matter; WM – white matter.

Table 3. Differences in volume of cortical and subcortical structures before and after 119.8 km race in ultra-trail group.

Volume (cm³)	Prerace (n=14) Mean±SD (Min–Max)		Postrace (n=14) Mean±Sd (Min–Max)		z	p
Brain total	1259.37±100.41	(1105.79-1421.54)	1274.74±102.25	(1128.13-1426.14)	-2.229	0.026*
CSF	271.50±46.89	(211.20-368.41)	272.82±51.45	(202.62-394.19)	-0.094	0.925
WM total	550.58±49.54	(493.15-658.62)	551.15±51.24	(467.51-659.81)	-0.534	0.594
GM total	723.59±59.66	(635.6-824.10)	738.12±33.75	(690.60-807.87)	-2.856	0.004*
Brainstem	25.91±2.22	(23-29.89)	26.07±2.25	(23.07-29.80)	-1.507	0.132
Cerebrum total	1104.69±97.12	(963.51-1262.35)	1110.88±58.38	(1037.74-1189.61)	-2.040	0.041*
Cerebrum WM	493.78±48.74	(440.07-604.71)	494.97±48.91	(422.67-605)	-0.596	0.551
Cerebrum GM	595.99±352.12	(514.14-981.02)	609.70±55.75	(522.80-706.86)	-2.856	0.004*
Cerebellum	143.68±13.43	(123.37-168.98)	143.97±13.75	(121.75-167.51)	-0.377	0.706
Thalamus	11.96±1.44	(10.09-15.55)	12.19±1.46	(10.2-15.83)	-2.606	0.009*
Caudate	7.78±1.10	(6.48-10.45)	7.92±1.19	(6.45-10.9)	-2.041	0.041*
Putamen	9.09±1.57	(6.62-12.83)	9.29±1.59	(6.65-13.13)	-1.917	0.055
Pallidus	2.62±0.29	(2.27-3.45)	2.71±0.32	(2.47-3.7)	-2.638	0.008*
Hippocampus	8.75±0.94	(6.95-10.31)	8.85±0.92	(7.09-10.46)	-3.305	0.001*
Amigdala	1.89±0.25	(1.48-2.29)	1.91±0.25	(1.55-2.34)	-0.420	0.672
Accubens	0.74±0.14	(0.48-0.95)	0.74±0.12	(0.51-0.93)	.000	1.00

* Significant differences at p<0.05. CSF – cerebrospinal fluid; GM – gray matter; WM – white matter.

program (SPSS version 25.0, IBM Corp.: Armonk, NY, USA). The Wilcoxon signed-rank test was used to determine differences in brain volume after the race in ST and UT groups, separately. The alpha value was accepted as p<0.05.

Results

Descriptive Participant Statistics

A total of 1207 runners (715 male and 492 female) departed for the ST (**Figure 1**), and 363 runners (324 male and 39 female) departed for the UT (**Figure 2**) route. Twelve runners in the ST and 15 runners in the UT were scanned before the race. Only 9 runners in ST and 14 runners in UT were scanned after the race. Four runners were excluded because of muscle injuries (*n*=2) or drop-out (*n*=1), and 1 runner in the UT group refused to participate in post-race measurements.

All participants were experienced but non-professional athletes with an average running history at least 2 years and were identical in terms of weight, height and BMI in both ST and UT groups. Although average running distance per year and per week was greater in the UT group compared to the

ST group, both groups were adapted long-term to endurance running. Although the average training volume was twice as high in the UT group compared to the ST group, performance expressed as running speed in training and race did not differ between the ST and UT groups. Descriptive data and characteristics of athletes are given in **Table 1**.

Volumetric Changes in Cortical and Subcortical Brain Regions Following the Marathon and the Ultramarathon Race

Pre- and post-race brain volumes of cortical and subcortical structures in ST (**Table 2**) and UT (**Table 3**) groups were evaluated, separately. According to the Wilcoxon signed-rank test, total brain volume increased significantly after the race in the UT group (Z=-2.23; p=0.026), but not in the ST group (Z=-1.36; p=0.173) when pre-race values were compared with post-race values (**Figure 3**).

A statistically significant increase in tissue volume was observed in total GM volume in both the ST (Z=-2.31; p=0.021) and the UT (Z=-2.86; p=0.004) groups (**Figure 4**), whereas the volume of WM, CSF and brainstem did not change between pre- and post-race values in either group (**Tables 2, 3**).
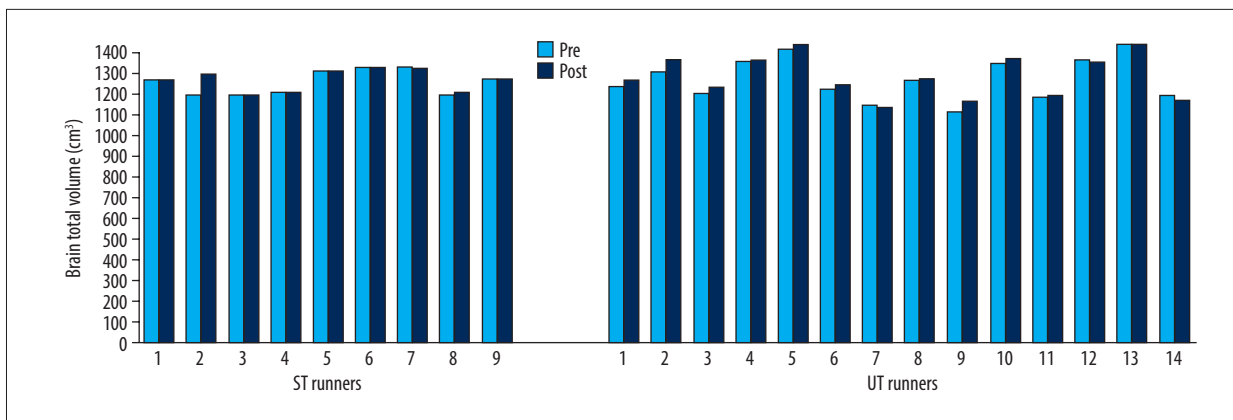
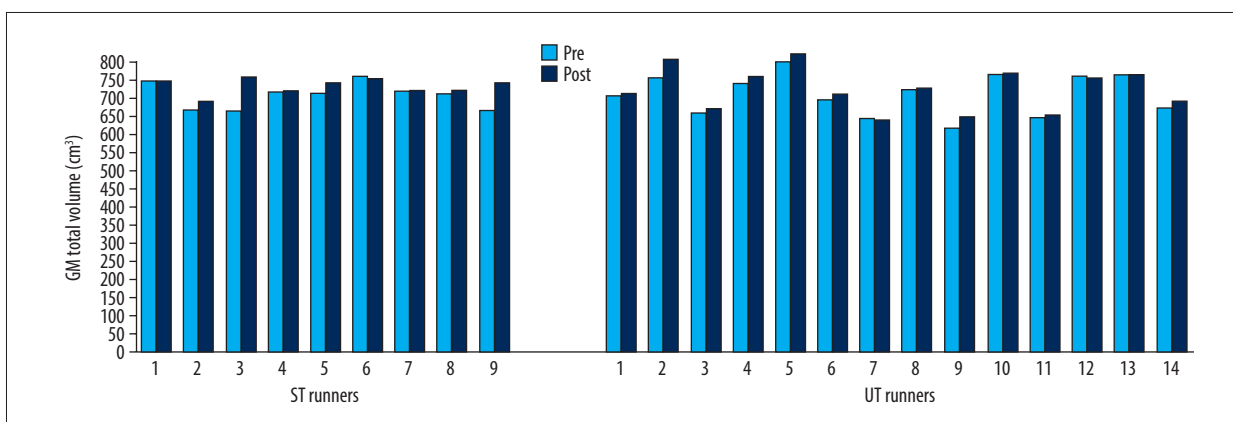**Figure 3.** Brain total volume changes in ST and UT group for each runner.

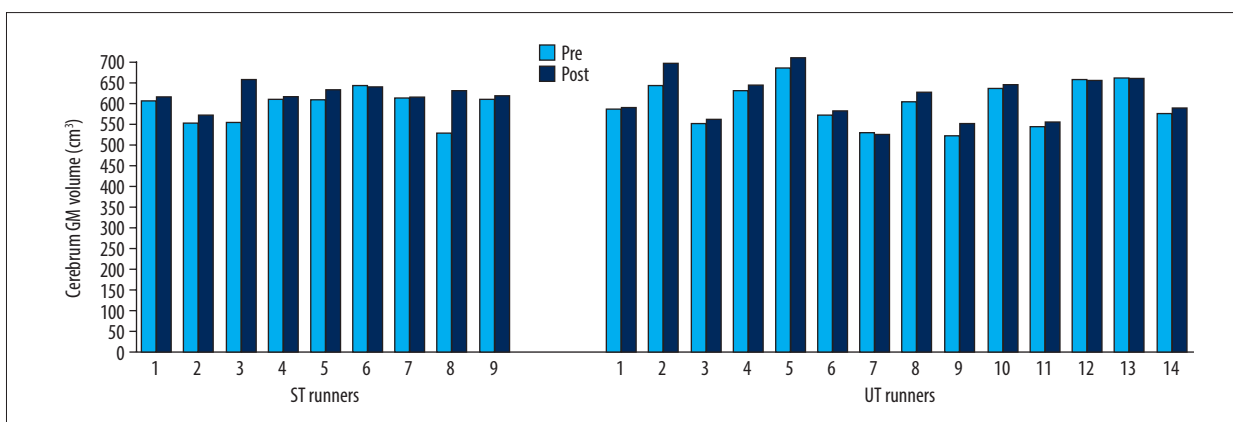**Figure 4.** GM total volume changes in ST and UT group for each runner.

Figure 5. Cerebrum GM volume changes in ST and UT group for each runner.

The cerebral GM volume was significantly higher after the race in both ST (Z=-2.31; p=0.021) and UT (Z=-2.86; p=0.004) groups (**Figure 5**).

On the other hand, total cerebral volume increased significantly between pre- and post-race in the UT group (Z=-2.04; p=0.041) but not in the ST group (Z=-1.72; p=0.086) (**Figure 6**).

Volume of cerebrum WM and cerebellum remained same and did not change in either group (**Tables 2, 3**).

Volumes of the thalamus (Z=-2.61; p=0.009) (**Figure 7**), caudate (Z=-2.41; p=0.041) (**Figure 8**), pallidus (Z=-2.64; p=0.008) (**Figure 9**), and hippocampus (Z=-3.31; p=0.001) (**Figure 10**) increased significantly after the UT race, whereas putamen, amygdala, and accumbens volumes did not change in the UT
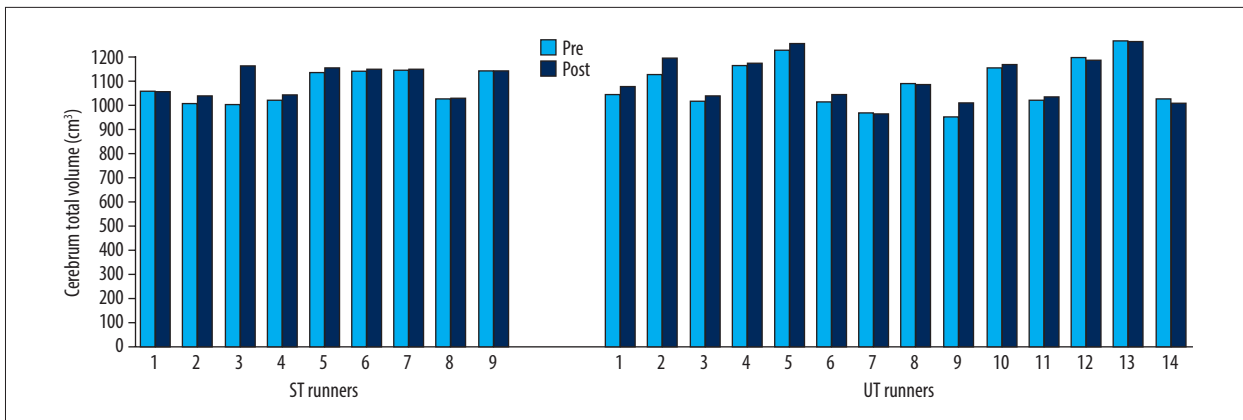
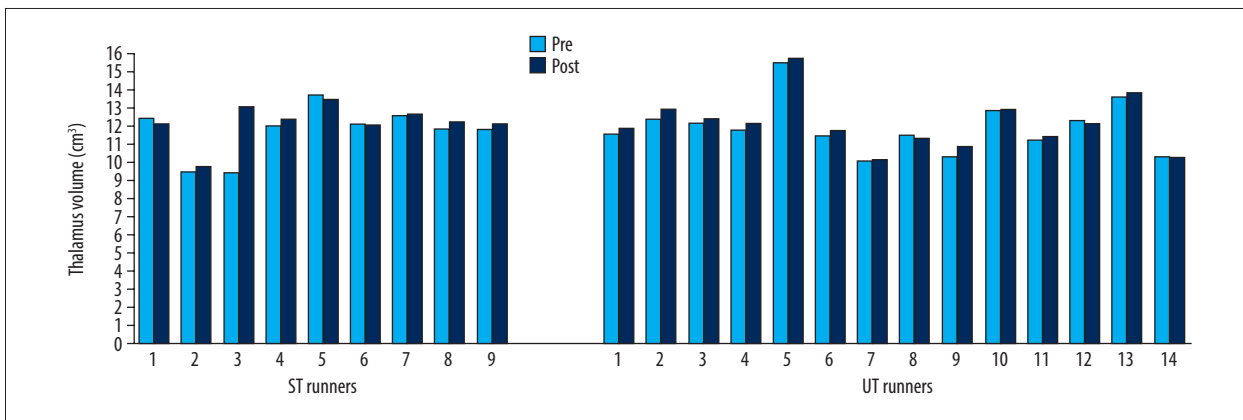**Figure 6.** Cerebrum total volume changes in ST and UT group for each runner.

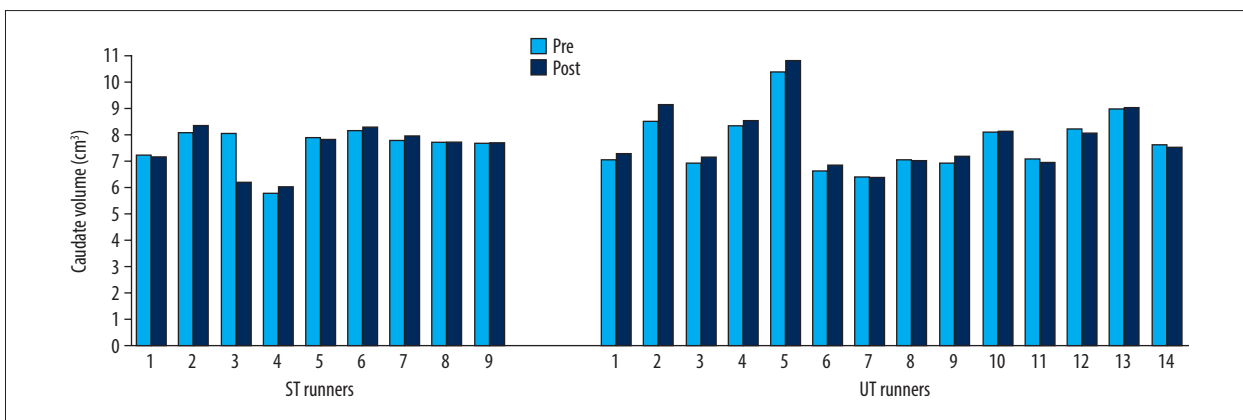**Figure 7.** Thalamus volume changes in ST and UT group for each runner.

Figure 8. Caudate volume changes in ST and UT group for each runner.

group. In the ST group, volumes of all subcortical structures remained unchanged when pre-race values were compared to post-race values (**Table 2**).

Discussion

This study assessed the acute impact of marathon and ultramarathon running on brain volume by using high-resolution 3-Tesla MRI scanning in older adult male athletes. We assumed that running distance may play a differential role and cause various physical and mental stress, giving rise to changes in the brain structures of male runners. We found a clear
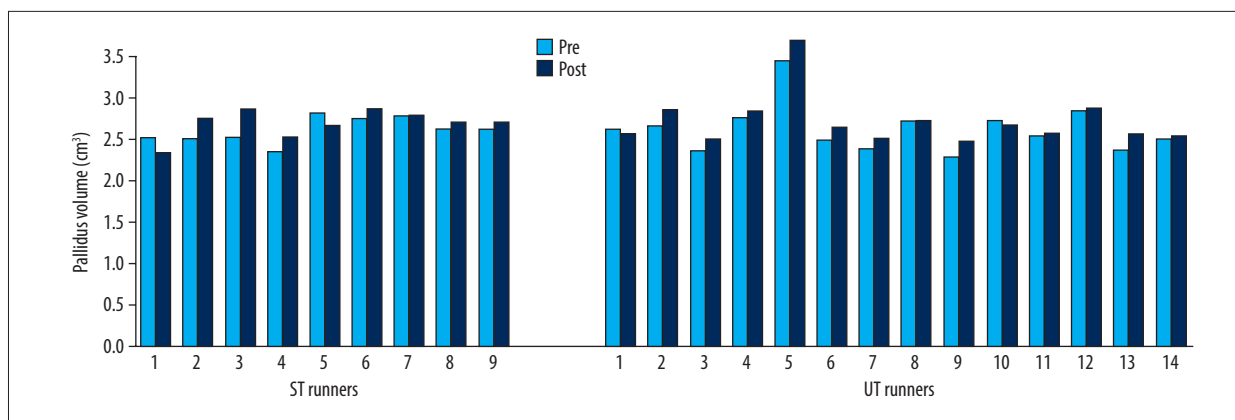
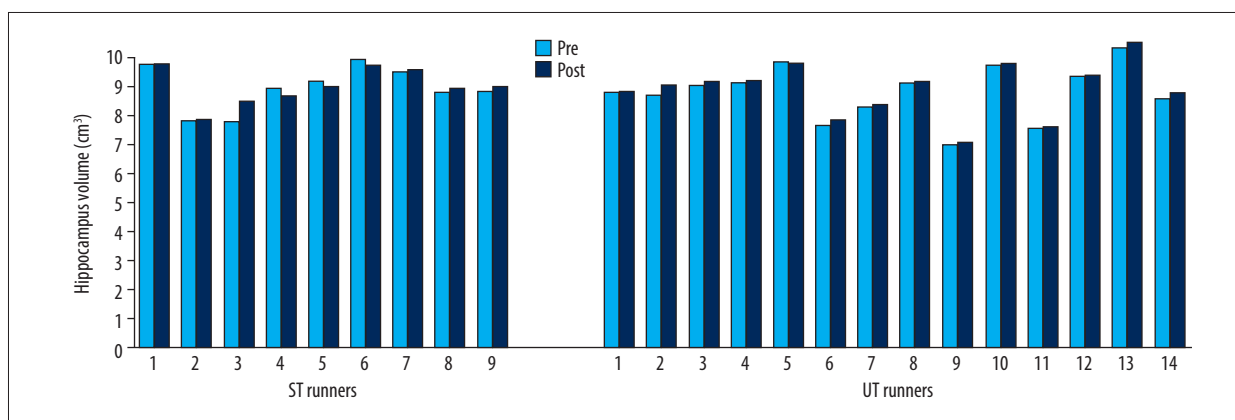**Figure 9.** Pallidus volume changes in ST and UT group for each runner.

Figure 10. Hippocampus volume changes in ST and UT group for each runner.

increase in total cerebral GM volume after the marathon and ultramarathon, whereas CSF, brainstem, and WM volumes did not change in either group. Moreover, volumetric increases in the thalamus, caudate, pallidus, and hippocampus after ultramarathon, but not marathon, running suggests that the response of brain tissue volume depends on running distance and exercise amount.

The acute increase in the GM, but not WM, volume after endurance running demonstrates that GM is more sensitive to exercise compared to WM tissue. This finding is similar to the results of the study focusing on long-term adaptation of ultramarathon in brain tissue of experienced athletes. Runners with experience of over 30 years had higher total GM volumes compared to physically active athletes, but WM volume did not differ between groups [32]. There is evidence that brain morphology can be altered in highly trained individuals within days to weeks as compared to normal individuals. Studies also demonstrated that GM volume is greater in regions of the brain related to skill and expertise as shown in professional musicians [37] and for various athletes such as golfers [38], judokas [39], and divers [40].

On the other hand, Freud et al reported a 6% total reversible GM volume decline among athletes during a multi-step ultramarathon with a total distance of 4487 km in 64 days [34]. The decrease in GM volume was correlated to body weight loss in athletes during the race. Moreover, Freud argued that volume change in cerebral cortex could be explained by long-term exposure to stress such as hyponatremia, which is known to have a negative effect on brain structure [41,42]. However, the increase in cerebral GM volume seems to be unrelated to hyponatremia [43] and/or hypernatremia [44], since WM volume changes accompany GM volume changes during hyponatremia or hypernatremia as a result of serum osmolality changes [45]. The increase in total GM volume may be due to mild hypoxia as a result of total altitude change during UM races, but not marathon races (3370 m and 1120 m, respectively). However, Rupp et al [46] demonstrated higher GM and WM volumes after prolonged exercise compared to 10-h rest under hypoxic conditions. While changes in WM volume were correlated with arterial oxygen saturation and are explained as a result of hypoxia, GM volume remained the same during rest under hypoxic conditions. Rupp et al suggested that although it is not caused by hypoxemia, hypoxic exposure causes some disturbances of brain function such as increased GM volume. These

studies together may suggest that endurance running has a greater impact on total GM compared to WM, and may provide a benefit in GM volume reserve, which is reported to decrease by 2% annually in sedentary males during aging [47,48].

Findings showed that hippocampus, basal ganglia, and thalamus components such as caudate and pallidus had greater volumes after the race in the UT group, whereas volumes of other brain structures were unchanged. These findings appear to agree with previous studies suggesting that some brain regions are more sensitive to exercise, especially ones that are prone to age-dependent atrophy [49,50]. Hippocampal and parahippocampal GM volume of the endurance athletes were significantly higher compared to performance athletes, which suggests that they cause changes in the motor learning and planning areas of the brain [51].

The present study showed that strenuous endurance exercise affects brain structures that were previously reported to be affected by aerobic exercise. In a cross-sectional study, it was shown that the higher the cardiorespiratory level, the larger the basal ganglia volume, which is related with better cognitive function performance [52]. Similarly, another study noted that caudate volume is closely related to the level of cardiorespiratory fitness and cognitive functions. Therefore, it can be predicted that an individual with higher cardiorespiratory fitness is more likely to have higher accuracy in task-switching [53]. The increase in cardiovascular fitness level and hippocampal volume due to exercise suggests that hippocampal volume plays a role in the fitness-spatial memory relationship [54]. A longitudinal study with 299 elderly subjects showed that greater physical activity above a threshold could double hippocampal volume in seniors [54]. Animal studies have demonstrated proliferation and survival of new neurons [55] and new vasculature [56] in the hippocampus after running exercise. Adult hippocampal neurogenesis was positively correlated to running distance and exercise duration in rats [57] with superior learning rates compared to sedentary animals [58].

Previous research showed that the caudate and putamen are activated differently during motor learning [59]. While the caudate usually plays a role in the beginning of motor learning, the putamen plays an active role in the automation of movements [60,61]. The globus pallidus, on the other hand, is a major component of the basal ganglia, which is responsible for the regulation of subconscious and voluntary movements [62]. Therefore, continuous changes in coordinative movements will result in some changes in cognitive functions [63] and might cause volumetric increase in some areas of the brain. The increased volume of caudate, pallidus, and thalamus in the current study might be explained by the requirement of adaptive tasks during outdoor running, which requires greater effort for balance and coordination compared to treadmill running.

The basal ganglia play a role in cognitive function through dopaminergic projections [64]. Therefore, it makes sense to assume that exercise causes upregulation of basal ganglia dopaminergic neurotransmission [65,66] and thereby improves cognitive processes after exercise. Interestingly, the fact that there was increased volume of the hippocampus, thalamus and basal ganglia in the UT group but not in the ST group indicates that there may be other factors in addition to exercise that affected brain-tissue volume alteration in this study. The UT group, but not the ST group, experienced sleep deprivation during the ultramarathon race, which lasted 24 hours. In 2019, Won et al showed that there was a relationship between executive functions and sleep and acute exercise, and that basal ganglia and caudate volumes are decisive in this interaction [67]. Studies have shown that sleep deprivation in rats decreased cell proliferation in the dentate gyrus of the hippocampus following a 96-hour treadmill exercise [68]. Findings of a similar study showed parallel results of neural effect [69]; however, the contribution of exercise volume and physical stress to neural effect has not been identified, since the effects of exercise and sleep deprivation are very similar. Conceptualizing the literature with the present results, it might be speculated that exercise amount and sleep deprivation in UT may produce different acute effects on the hippocampus, basal ganglia, and thalamus compared to ST, and further studies are needed to examine the interactive long- and short-term effects of sleep and endurance exercise on brain structure and function.

Although this study reports many valuable findings, it also has some limitations. First, we emphasize that our small sample was limited to healthy male older adult runners; thus, our findings may not be generalized to younger runners. Second, our findings are representative for single-stage ultramarathons at the distance of 120 km. Thus, findings cannot be generalized to all ultramarathon races because of their great diversity and additional extreme conditions such as weather, distance, and nature of the race. Moreover, the study was observational, and fluid and energy intake were not controlled during the international race. The restrictions of athletes from taking a shower right after the race and taking them to the MRI scan without any delay were tightly controlled to avoid any changes in the brain structures. Variables that may affect cortical thickness such as daytime sleepiness were not controlled in the observational study [70]; however, time-matched scanning procedure has been performed to lighten these alterations in brain volumes [71]. Although prior power analysis was performed, dropouts during the race caused a decline in the power of the study. Since evaluation of the acute effect of ultramarathon running on cortical and subcortical structures in the brain is sporadic, we compared our results with the current literature that is based on animal studies or long-term adaptations in human subjects. Both are insufficient to conclude specific outcomes, and further studies are needed to clarify the underlying mechanisms.

Conclusions

This study presented for the first time the acute effect of endurance running at 38.6 km and 119.8 km on the volume of cortical and subcortical brain structures by using high-resolution 3-Tesla MRI scanning. It can be concluded that single-stage endurance running event can cause increased cerebral GM volume in both short-trail and ultra-trail races. On the other hand, the increase in the volumes of the thalamus, caudate, pallidus, and hippocampus in the UT group, but not the ST group, might suggest that other variables such as sleep deprivation in addition to exercise may be crucial during UM running that extends beyond daylight hours into the night. It can be concluded that endurance running can help to preserve GM volume in male runners and suggests a method for prevention of stress or age-related GM decline. However, more detailed studies are needed to examine the cause of brain volume changes depending on both physical activity and physical stress experienced during ultramarathon running.

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