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# Effects of repeated unihemispheric concurrent dual-site tDCS and virtual reality games on motor coordination of sedentary adolescent girls

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## Abstract

**Background** This study investigated the effects of repetitive unihemispheric concurrent dual-site anodal transcranial direct current stimulation (a-tDCS$_{UHCDS}$) associated with the use of virtual reality games (VR) on the motor coordination of sedentary adolescent girls.

**Methods** Thirty-six inactive adolescent girls were randomly assigned into 3 groups ($n = 12$ per group): (1) VR + a-tDCS$_{UHCDS}$, (2) VR + sham-tDCS$_{UHCDS}$, and (3) Control. The VR + a-tDCS$_{UHCDS}$ and VR + s-tDCS$_{UHCDS}$ groups received the intervention three times a week for four weeks. In each experimental session, participants first received either 20 min of a-tDCS$_{UHCDS}$ (2 mA at each anodal electrode) targeting the primary motor cortex (M1) and the left dorsolateral prefrontal cortex (DLPFC) or sham and then performed VR for 1 h. The control group received no intervention. Eye-hand coordination (EHC) and bimanual coordination (BC) were measured at baseline, post-intervention, and two weeks later (retention test) using the automatic scoring mirror tracer and continuous two-arm coordination test, respectively.

**Results** Results showed that the EHC was significantly higher in the VR + a-tDCS and VR + s-tDCS groups at post-intervention (*all ps* $< 0.001$) and the retention test (*all ps* $< 0.001$) compared to the control group. Moreover, the EHC was significantly higher in the VR + a-tDCS group compared to the VR + s-tDCS group ($p = 0.024$) at the retention. Similarly, VR + a-tDCS and VR + s-tDCS improved BC compared to the control group at post-intervention (*all ps* $< 0.001$) and retention test (*all ps* $< 0.001$). In addition, higher BC was observed in the VR + a-tDCS group compared to the VR + s-tDCS group ($p < 0.001$) at the retention test.

**Conclusions** Our results suggest that adding a-tDCS$_{UHCDS}$ to VR over 12 sessions may have an additional effect on VR training for improving and retaining motor coordination in sedentary adolescent girls.

**Keywords** Bimanual coordination, Eye-hand coordination, Sedentary adolescent girls, Transcranial direct current stimulation, Virtual reality

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## Background

During adolescence, a considerable proportion of leisure time is spent engaged in sedentary activities, which are defined as waking behaviors characterized by tasks with low energy expenditure (<1.5 metabolic equivalents of task; MET) [1]. Given the significance of the physical, emotional, mental, and developmental changes that occur during adolescence, regular physical activity (PA) can facilitate the development of an active lifestyle and, to some extent, ensure appropriate participation in future activities [2, 3]. It is therefore recommended that adolescents engage in at least 60 min of moderate to vigorous PA daily [4]. However, recent reports have indicated that approximately 77.6% of boys and 84.7% of girls aged 11 to 17 years do not engage in the recommended amount of PA [5]. Furthermore, the levels of PA exhibit a notable decline during the adolescent period [6].

Coordination abilities are among the essential needs for physical skills that allow a person to use neuromuscular and motor coordination of the muscles and body segments/limbs for a successful and accurate execution of any motor task [7]. In particular, there is evidence of a reciprocal effect between PA and coordination abilities, whereby lack of coordination may contribute to a reduced willingness to engage in PA, and such a decrease in PA negatively affects coordination abilities [8]. Eye-hand coordination (EHC) is the ability to perform activities that require the simultaneous use of both hands and eyes to collect information from the visual field and to guide the hands to achieve a desired outcome. [9]. EHC is a fundamental component of numerous daily activities, including but not limited to tool use, food preparation, exercise, and work [10]. Normal EHC involves the synergistic functioning of several sensorimotor systems, including the visual system, vestibular system, proprioception, and eye, head, and arm control systems, as well as attention and other cognitive aspects [7]. Studies have shown that early acquisition of the EHC skill leads to improvements in fitness, body image, and participation in sport [11].

Bimanual coordination (BC) is another vital aspect of coordination skills, which is very important for performing daily activities and also for engaging in PA [12]. BC skills require a well-coordinated interplay between the upper extremities, which is controlled by several brain areas such as the primary motor cortex (M1), supplementary motor cortex, premotor cortex, cingulate and posterior parietal cortex, and dorsolateral prefrontal cortex (DLPFC) [13–15]. Successful performance of bimanual tasks depends not only on the spatio-temporal synchrony of the movements of the two hands but also on visual feedback and EHC patterns [16]. This is particularly evident during the terminal phase of a bimanual task when temporal symmetry breaks down and different patterns of EHC emerge [16]. This shows the link between EHC and BC and their interplay in coordination abilities.

Considering the reciprocal effect between PA and coordination skills, the development of new strategies to increase engagement in the PA and also enhance coordination abilities such as EHC and BC has received attention. Virtual reality (VR) is a relatively new technology in which a simulated experience is created to give users an immersive feel of a virtual world [17]. Sport VR games have recently been recognized as a new strategy to increase PA and promote health benefits in healthy and clinical populations [18]. It has also been reported that sports VR games improve reaction time, EHC, motor control, and motor coordination, probably by enhancing visual perception and facilitating visual feedback cues in the environment [19–22]. Given the importance of early adolescence (12–17 years) as a critical period of growth and a cornerstone for establishing a healthy lifestyle, VR may be a promising intervention strategy for engaging adolescents in physical activity and improving motor function [23]. Recently, VR and other so-called "exergames" (i.e., video games that involve physical exertion) have been widely used by children and adolescents, and this new generation of games may help to increase PA and reduce sedentary lifestyles [24]. VR increases the amount of energy that children and adolescents spend on video games and allows them to increase their PA, which also has the potential to overcome barriers to participation in real-world PA [25]. Recent evidence suggested positive effects of VR on motor function in children and adolescents [26–28]. Wing et al. [26] reported an improvement in EHC with VR among elementary school children. Caro et al. [27] also investigated the effects of VR on improving eye-body coordination in children with autism and found that children with severe autism kept their attention for the entire duration of treatment, reduced aimless limb movements, and improved limb movements as a result of exergaming. They also found that exergaming can be effective for children with autism in improving eye-body coordination, especially in helping to develop limb movements [27].

In addition, many researchers are trying to design and devise new intervention methods to make training sessions more productive and increase the ability to execute and learn motor tasks [29]. Non-invasive brain stimulation (NIBS) is one of the growing strategies in this regard and has been gaining attention over the last two decades [30, 31]. In particular, Transcranial Direct Current Stimulation (tDCS), which is the most common NIBS technique, has shown promising results for improving cognitive and motor function in different target populations [32–34]. tDCS induces its effects by passing a direct current up to 4 mA through the skull using at least two electrodes (anode and cathode), which may modulate the neuronal excitability of different areas of the brain [35–38]. Although applying a smaller and more focal target electrode, and a larger reference electrode is gaining popularity in recent tDCS studies, the most frequently used electrode sizes are between 25 and 35 $cm^2$ [39]. In this regard, M1 and DLPFC are the most common areas investigated in previous studies mostly because of their substantial role in regulating exercise and cognitive function [40–43]. Indeed, various studies have shown that stimulating either M1 or DLPFC improves various aspects of exercise performance and cognition [41, 44–48]. Interestingly, recent findings have shown that the activation of M1 and DLPFC areas can be effective in learning movement skills and its underlying neurophysiological mechanisms are related to the changes in neuronal excitability, neurotransmitters, synaptic plasticity, and brain network functional connections [49]. It has also been reported that anodal tDCS over the M1 area results in faster skill acquisition [50]. Accordingly, the anodal unihemispheric concurrent dual-site tDCS (a-$tDCS_{UHCDS}$) was recently proposed as an effective strategy for simultaneously stimulating M1 and DLPFC, yielding a greater increase in corticospinal excitability compared to the isolated stimulation of M1 and DLPFC [51–53]. It is noteworthy that this increase in corticospinal excitability has been shown to last for 24 h after a-$tDCS_{UHCDS}$ [51]. Talimkhani et al. [54] provided further support for the effectiveness of a-$tDCS_{UHCDS}$ by showing its positive effect on the acquisition of cognitive skills and functions in healthy subjects.

Considering that both VR and tDCS may improve different facets of cognitive and motor function, one could speculate that adding a-$tDCS_{UHCDS}$ to VR training could provide a synergistic effect leading to more positive and long-lasting outcomes, particularly in a sensitive population like adolescent girls. To fill this gap, we aimed to investigate the effects of the concurrent application of a-$tDCS_{UHCDS}$ and VR on motor coordination in sedentary adolescent girls. We hypothesized that the addition of a-$tDCS_{UHCDS}$ to the VR protocol would result in an enhancement in motor coordination, as measured by EHC and BC, compared to the use of sham-tDCS with the VR protocol in sedentary adolescent girls.

## Materials and methods

### Study design

This study was a single-blinded and sham-controlled randomized controlled trial with three parallel groups (between-subject design), conducted within four weeks. The study protocol was pre-registered in the Iranian Registry of Clinical Trials *(IRCT id: IRCT20221124056598N1)* and was approved by the Ethics Committee of Razi University *(IR.RAZI.REC.1401.058)*. All the experimental procedures were conducted following the declaration of Helsinki. Written informed consent was obtained from the parents of the subjects before participating in the study.

First, in a familiarization session, the subjects got acquainted with the whole experimental procedure, interventions, and measuring outcome variables. In this session, anthropometric characteristics such as height and weight were also measured. The height and weight of each subject were employed to calculate the body mass index (BMI) for subsequent comparisons. Then, the pre-test measurements including EHC and BC were conducted. Following the pre-test, the subjects were randomly assigned to one of the three experimental groups including (1) VR+a-$tDCS_{UHCDS}$, (2) VR+sham-tDCS (s-$tDCS_{UHCDS}$), and (3) Control, each containing 12 participants. The VR+a-$tDCS_{UHCDS}$ and VR+s-$tDCS_{UHCDS}$ took part in a four-week protocol including three sessions per week (12 sessions in total). In each session, the VR+a-$tDCS_{UHCDS}$ group first received 20 min of anodal $tDCS_{UHCDS}$ followed by the VR. The VR+s-$tDCS_{UHCDS}$ followed the same approach except that they received 20 min of sham stimulation before VR in each session. The participants in the control group were asked to maintain their usual routines (i.e., their usual activities of daily living) and did not receive any form of intervention. They only participated in the outcome measures assessment. The study variables were measured at baseline (pre-test), 24 h after the intervention phase (after 4 weeks), and 2 weeks after the termination of the intervention phase as the retention test.

### Participants

Thirty-six sedentary adolescent girls participated in the present study. The sample size was calculated using G*Power software (Version 3.1.9.2, Kiel, Germany) as follows: test family=F tests; Statistical test=ANOVA: Repeated measures, within-between interaction; $\alpha$ error probability=0.05; power (1-$\beta$ err prob)=0.80; Effect size f=0.3, number of groups=3, number of measurements=3, Correlation among repeated measures=0.5, Nonsphericity correction $\varepsilon$ = 1. The effect size used for calculating the sample size was derived from a review article in which the effect of tDCS on motor learning and memory performance was evaluated [55]. Accordingly, 27 participants would be appropriate as the sample size for the present study. Considering the possibility of dropouts considering the number of sessions and their duration and the whole study procedure [56], 36 participants were recruited for this study. Interestingly, there were no dropouts, and all the participants from the initial pool completed the whole experimental procedure. Inclusion criteria were: (a) being a sedentary girl based on the International Physical Activity Questionnaire (IPAQ), (b) aged 15–18 years, (c) being right-handed, and

(d) having a normal or corrected vision. Also, the exclusion criteria were: (a) having a history of neurological disease, (b) having cardiovascular disease, (c) having any metal implants in the brain, (d) a history of disturbance in balance, recurrent postural dizziness, and fear of electrical stimulation of the brain, (e) failure to adhere to the study's instructions, including participation, interventions, and measurements during testing, (f) any weakness or physical injury, and (g) inability to finish test and exercise sessions. The characteristics of the participants are presented in **Table 1**.

### International physical activity questionnaire (IPAQ)

IPAQ was used to evaluate the level of PA. This questionnaire is a short version of IPAQ and has both acceptable validity and reliability [57, 58]. According to the scoring procedure of the IPAQ, participants who scored less than "600 MET minutes a week" were identified as sedentary (low level of physical activity) and participated in this study. Further detailed information regarding the scoring and analysis of the IPAQ can be found at www.ipaq.ki.se. IPAQ was used only for the participants' screening process.

### Randomization and allocation concealment

In this study, permuted block randomization was conducted via the www.randomization.comwebsite. This involved first allocating a unique number to each subject as an identification code, followed by the generation of a sequence of 36 digits (equivalent to the sample size). Treatment labels were then defined in the relevant section of the website, comprising: 1) VR+a-tDCS$_{UHCDS}$, 2) VR+s-tDCS$_{UHCDS}$, and 3) Control groups. Once the treatment groups had been defined, a permuted block randomization procedure was employed to mitigate potential issues associated with equal block sizes. In this instance, the block sizes were not equal and were instead multiples of the number of treatment groups (e.g., block sizes of 2, 4, 6, or 8). The website could randomly specify the sequence of blocks with different sizes. In the final step, the '*Generate Plan*' function on the website was employed to randomly assign subjects to blocks of different sizes, which already had a random sequence. Finally, the group to which each subject belonged was determined by cross-referencing the subject number (identification code) with the blocks.

### Transcranial direct current stimulation (tDCS)

tDCS was applied using two battery-driven stimulator devices with two channels each (NeuroStim 2, Medina Tebgostar, Tehran, Iran). Four carbon electrodes, two anodes (5×4 cm; 20 cm2; 0.10 mA/cm² each), and two cathodes (9×4; 36 cm2; 0.056 mA/cm²) electrodes, covered by saline-soaked surface sponges (NaCl 140 mmol dissolved in Milli-Q water) were used to concurrently stimulate target areas in the brain. The larger cathode electrodes were chosen to decrease the neuromodulatory effects of these electrodes. A 64-channel EEG cap with the international 10–20 EEG system positions was used to locate target areas over the scalp. The a-tDCS$_{UHCDS}$ montage was used for simultaneously targeting M1 and DLPFC areas [52, 54]. a-tDCS$_{UHCDS}$ was applied before VR training with 2 mA at each nominal target (i.e., 2 mA at M1 and 2 mA at DLPFC) for 20 min. One anode electrode was placed symmetrically over the Cz (2.5 cm on each side of the M1) targeting the motor cortex and the other anode electrode was placed vertically over F3 targeting the left DLPFC. The cathode electrodes were placed vertically over the supraorbital region, centered at AF4 and the other centered between Fpz and AFz. This montage was chosen based on recent studies showing that a-tDCS$_{UHCDS}$ is an effective strategy for simultaneous stimulation of M1 and DLPFC yielding higher and long-lasting corticospinal excitability compared to the isolated stimulation of M1 and DLPFC [51, 54]. In both a-tDC$_{SUHCDS}$ and sham tDCS conditions, the current was gradually ramped up and down at the beginning and end of stimulation for 30 s. In a-tDCS$_{UHCDS}$, the current was maintained at 2 mA for 20 min. In the sham condition (s-tDCS$_{UHCDS}$), the same electrode position was applied, but the 2-mA current was maintained only for 30 s. This protocol is adequate for blinding participants in tDCS studies [33, 59–61].

### tDCS modeling

The computational modeling of the a-tDCS$_{UHCDS}$-induced electric current in the brain was performed following a previous study [53]. The brain current flow during tDCS was calculated using a finite element model (FEM) following the standard pipeline in SimNIBS 4.0.0 [62]. The magnetic resonance imaging (MRI) head model template from the Montreal Neurologic Institute (MNI 152) available in the software was used for the simulation.

**Table 1** Average age, height, and Weight in three groups (Mean ± SD)

| Groups | Age $_{(year)}$ | Height $_{(cm)}$ | Weight $_{(kg)}$ | BMI $_{(kg/m^2)}$ | PA Level $_{(MET/Min/Week)}$ |
|---|---|---|---|---|---|
| VR + a-tDCS | 16.08 ± 1.00 | 159.00 ± 7.45 | 52.93 ± 8.21 | 20.94 | 241.00 ± 96.3 |
| VR + s-tDCS | 15.75 ± 0.97 | 159.67 ± 5.88 | 55.79 ± 10.55 | 21.88 | 276.9 ± 101.2 |
| Control | 16.17 ± 1.11 | 159.33 ± 5.50 | 55.80 ± 5.95 | 21.98 | 244.08 ± 66.3 |

VR+a-tDCS = virtual reality and anodal Transcranial Direct Current Stimulation; VR+s-tDCS = virtual reality and sham Transcranial Direct Current Stimulation; BMI = body mass index; PA = physical activity

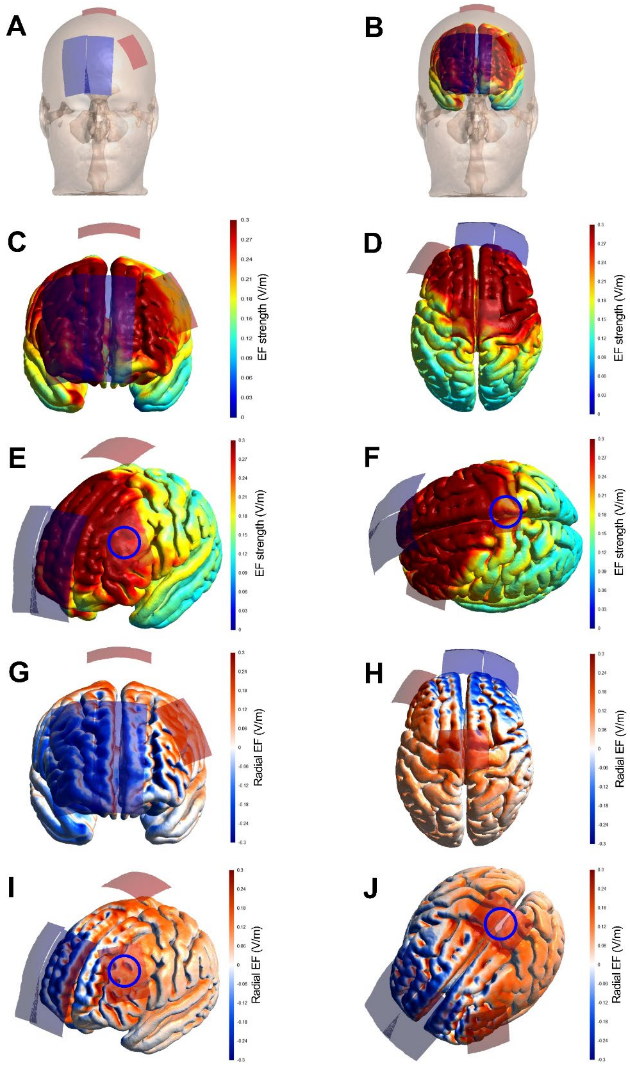


**Fig. 1** Strength and radial component of the electric field induced by tDCS, reproduced from Banaei et al. [53]
Finite Element Models derived from Magnetic Resonance Imaging in a head model (MNI152) of the strength and radial (normal to the cortical surface) component of the electric field (EF) induced by tDCS. Electrode montage targeting the simultaneous stimulation with anodal tDCS of the representation of the lower limbs in the primary motor cortex and the left dorsolateral prefrontal cortex (**A** and **B**), with red electrodes representing the anodes (5×4 cm) and blue electrodes representing the cathodes (9×4 cm). The EF strength is presented in the color-coded figures (**C**, **D**, **E**, and **F**), with hotter colors indicating stronger EF and colder colors indicating the opposite. The radial EF is presented in the color-coded figures (**G**, **H**, **I**, and **J**), where red color represents the electric current flowing into the cortex (i.e., inducing excitatory effects) and blue color represents the electric current flowing out of the cortex (i.e., inducing inhibitory effects). The study montage has reached the target areas with enough electric current strength to induce a neuromodulatory effect, as shown in figures **E** and **F** (blue circles roughly representing the target areas). Furthermore, the target areas were stimulated with the desired polarity (i.e., anodal current) to induce excitatory effects in the target regions, as shown in panels **I** and **J** (blue circles roughly representing the target areas)

MRI data were segmented into surfaces corresponding to the white matter (WM), gray matter (GM), cerebrospinal fluid (CSF), skull, and skin. The electrical conductivities of each segment were determined according to values previously established as follows: WM = 0.126 S/meter (S/m), GM = 0.275 S/m, CSF = 1.654 S/m, bone = 0.010 S/m, and skin/scalp = 0.465 S/m [63], rubber electrode = 29.4 S/m, and saline-soaked sponges = 1.000 S/m [63]. All information concerning the respective tDCS montages was entered into the software: current intensity = 2 mA for each anode; electrode position (+F3 and +Cz / -Fpz and -AF4); electrode and sponge sizes (anodes 5×4 cm and cathodes 9×4 cm); electrode thickness = 1 mm; sponge thickness = 5 mm. The results of the simulations are presented in **Fig. 1**, in terms of the electric field strength (**Fig. 1C**, **D**, **E**, ***and F***) and radial (**Fig. 1G**, **H**, **I**, ***and J***) electric field (normal to the cortical surface), both of which are most important for neuromodulatory effects of tDCS [64]. As can be seen in **Fig. 1C**, **D**, **E**, ***and F***, the study montage has reached our target areas with enough electric current strength to induce a neuromodulatory effect (>0.2–0.25 V/m) [65]. Furthermore, the target areas were stimulated with the desired polarity (i.e., anodal current) to induce excitatory effects in the target regions (**Fig. 1G**, **H**, **I**, ***and J***). Other areas such as the supplementary motor area, premotor cortex, and other prefrontal cortex were also stimulated in the current path from the anodal to the cathodal electrode. This spread electric current is a characteristic of tDCS applied with large rectangular pads (the so-called 'conventional' tDCS) [66]. The figure was reproduced from Banaei et al. [53] who used the same a-tDCS$_{UHCDS}$ as in the present study.

### Virtual reality

For VR we used Xbox Kinect, which is a commercial videogame console involving a combination of software and hardware (Xbox 360 and Kinect Xbox 360, Microsoft) connected to a television (47" LG). The hardware includes a system consisting of a projector, an infrared camera, and a special microchip. Kinect is a motion assessment device that no longer needs special clothing and sensor connectivity, and at the same time as the person moves, it transfers the position of the body to the device and the game, creating a connection between the real and virtual worlds [67]. The VR sessions were conducted three times per week, on non-consecutive days, over four weeks (12 sessions in total). In each session, the participants received 20 min of either a-tDCS$_{UHCDS}$ or sham, after which they proceeded to perform the VR session for 60 min. In this study, the Kinect sports games Skiing, Ping Pong, Boxing, and Golf were employed. Each game was played for 15 min, resulting in a total duration of 60 min for each VR intervention session. The order in which the four games were presented was not fixed; participants were permitted to select the order of the games according to their preferences. However, they were required to play all four games in each session. Each game was presented only once in a single session, and the VR intervention was conducted in a quiet, distraction-free environment.

#### Control group
The complete control group did not receive any intervention with tDCS (neither anodal nor sham) or VR. However, they underwent the same evaluation protocol at baseline (pre-test), after the intervention phase (after 4 weeks), and 2 weeks after the termination of the intervention phase as the retention test.

#### Eye-hand coordination (EHC) assessment
An Automatic Mirror Trace (Model 58024 A, Lafayette Instrument Company, Indiana, USA) device was used to measure the EHC. The validity of this device has already been proven [68, 69]. The device consisted of an aluminum plate with a nonconducting black star pattern anodized onto the surface, a metal plate, a mirror, and a metallic-tracing stylus. The aluminum plate and the metallic-tracing stylus were both connected to the Silent Impulse Counter (Model 58024 C, Lafayette Instrument Company, Indiana, USA). The metal plate was positioned above the surface in a way that the participants were just able to see their tracing hand through the mirror and not directly. The pertinent instructions were given to the participants to minimize errors and complete the task as fast as possible. The participants were then asked to position the stylus over the pattern and draw a star, both clockwise and counter-clockwise. A full clockwise and counter-clockwise drawing was considered one attempt. Each participant was asked to perform five attempts with their dominant hand, with one minute of rest between the attempts. During the task, touching the aluminum plate by the stylus (stylus outside of the star pattern) was defined as an error. The number of errors and the time to complete the task were used for calculating the score of each attempt using the following formula: *"Standard Score for Each Attempt = (100 – number of errors) / (completion time in seconds)".* The mean value of these five attempts was calculated as the total score of each participant and used for statistical analysis. Higher scores represented better EHC. The EHC was assessed at baseline (pre-test), after the intervention phase (after 4 weeks), and 2 weeks after the termination of the intervention phase as the retention test.

#### Bimanual coordination (BC) test
A Two-Arm Coordination Test device (Model 32532, Lafayette Instrument Company, Indiana, USA) was used to measure the BC. The validity of this instrument has been previously demonstrated [70]. The device consisted of a Tracing Apparatus connected to the Economy Clock/Counter (Model 54060 A, Lafayette Instrument Company, Indiana, USA). Participants were asked to sit directly in front of the two-arm tracing apparatus. The test was composed of two operations including tracing a star in a clockwise and a counter-clockwise direction. The participants were instructed on how to manipulate the stylus by moving the handles of the apparatus; spreading the handles made the stylus move toward the top of the board; bringing the handles together moved the stylus downward on the board. Lateral movement was also accomplished by simultaneously moving both handles to the left or the right. It was then explained to the participants that the objective of the test was to manipulate the handles in such a way as to keep the stylus on the black star pattern and move it around the star as quickly as possible, making as few errors as possible. A full clockwise and counter-clockwise drawing was considered one attempt. Each participant was asked to perform five attempts, with one minute of rest in between. During the task, touching the aluminum plate by the stylus (stylus outside of the star pattern) was defined as an error. The number of errors and the time to complete the task were used for calculating the score of each attempt using the following formula: *"Standard Score for Each Attempt = (100 – number of errors) / (completion time in seconds)".* The mean value of these five attempts was calculated as the total score of each participant and used for statistical analysis. Higher scores represented better BC. The BC was assessed at baseline (pre-test), after the intervention phase (after 4 weeks), and 2 weeks after the termination of the intervention phase as the retention test.

#### Statistical analysis
The statistical analyses were performed using SPSS software, version 23 (SPSS Inc., Chicago, IL, USA). The normal distribution of each data set was evaluated by the Shapiro-Wilk normality test. All data were normally distributed, and accordingly, a two-way mixed ANOVA test was employed for statistical analyses (a 3×3 factorial design, time as the within-subject factor with three levels, and group as the between-subject factor with three levels). When a significant interaction effect was observed, the Bonferroni-corrected post hoc test was applied for pairwise comparisons. In case of a violation in the assumption of sphericity, as assessed using the Mauchly test, the Greenhouse-Geisser epsilon correction was applied. Partial eta squared ($\eta^2_p$) was used as a measure of the effect size for the ANOVAs and interpreted as small (0.01–0.059), medium (0.06 to 0.139), or large (≥0.14). Cohen's d ($d_{av}$) calculation of the effect size was also used for pairwise comparison and interpreted as small (0.20–0.49), medium (0.50–0.79), or large (≥0.80). Moreover,

the "percentage difference" between the groups at each time $[(\%\Delta=100 \times \frac{|Mgroup1-Mgroup2|}{\frac{Mgroup1+Mgroup2}{2}}),\ M: mean]$ [71] and the "percentage change" within each group over time $[(\%\Delta=100 \times \frac{Mpost-Mpre}{Mpre}),\ M: mean]$ were calculated and reported as (%Δ). The significance level for all tests was defined as $p<0.05$. All values in the figures are presented as the mean ± standard deviation (M ± SD).

## Results

The mean values of the **EHC** of each experimental group at three specified time points (baseline, post-intervention, and retention) are presented in **Table 2**. The results showed significant main effects of group ($F_{(2,33)}=28.2$, $p< 0.001$, $\eta^2_p= 0.631$) and time ($F_{(2,66)}=153.07.3$, $p< 0.001$, $\eta^2_p= 0.823$), and also "group × time" interaction ($F_{(4,66)}=30.3$, $p< 0.001$, $\eta^2_p= 0.647$) on the **EHC**. Pairwise comparisons revealed that **EHC** improved significantly from baseline to post-intervention ($p< 0.001$, $d_{av}= 4.3$, $\Delta= +325.5\%$ and $p< 0.001$, $d_{av}= 2.6$, $\Delta= +208.5\%$) and retention test ($p< 0.001$, $d_{av}= 5.1$, $\Delta= +360.4\%$ and $p< 0.001$, $d_{av}= 2.8$, $\Delta= +221.2\%$) in the VR + a-tDCS and VR + s-tDCS group, respectively, while no significant change was observed from the post-intervention to the retention test in both groups ($p> 0.05$). Pairwise comparisons also demonstrated that the **EHC** was significantly higher at post-intervention in the VR + a-tDCS and VR + s-tDCS groups than the control group ($p< 0.001$, $d_{av}= 3.1$, $\Delta=103.7\%$; $p< 0.0001$, $d_{av}= 2.4$, $\Delta=85.7\%$, *respectively*). Also, at the retention test, the **EHC** was significantly higher in the VR + a-tDCS compared to both the VR + s-tDCS ($p=0.024$, $d_{av} = 1.04$, $\Delta=26.9\%$) and control ($p< 0.001$, $d_{av}= 3.8$, $\Delta=104.6\%$) groups. The **EHC** was also significantly higher in the VR + s-tDCS group compared to the control group ($p< 0.001$, $d_{av}= 2.2$, $\Delta=83.5\%$) at the retention, **Fig. 2***(A)*.

The mean values of the **BC** of each experimental group at three specified time points (baseline, post-intervention, and retention) are presented in **Table 2**. The results demonstrated that there were significant main effects of group ($F_{(2,33)}=37.5$, $p< 0.001$, $\eta^2_p=0.695$) and time ($F_{(2,66)}=113.7.3$, $p< 0.001$, $\eta^2_p= 0.775$), and also "group × time" interaction ($F_{(4,66)}=30.4$, $p< 0.001$, $\eta^2_p= 0.649$) on the **BC**. Pairwise comparisons revealed that **BC** improved significantly from baseline to post-intervention ($p< 0.001$, $d_{av}= 3.4$, $\Delta= +114.6\%$ and $p< 0.001$, $d_{av}= 2.6$, $\Delta= +112.1\%$) and to the retention test ($p< 0.001$, $d_{av}= 4.7$, $\Delta= +168.5\%$ and $p< 0.001$, $d_{av}= 2.1$, $\Delta= +82.9\%$) in the VR + a-tDCS and VR + s-tDCS group, respectively. **BC** was also improved significantly from post-intervention to the retention test ($p=0.008$, $d_{av}= 0.9$, $\Delta= +25.1\%$) in the VR + a-tDCS but not in the VR + s-tDCS group ($p> 0.05$).**BC** was also significantly higher at post-intervention ($p< 0.001$, $d_{av}= 3.1$, $\Delta=79.8\%$ and $p< 0.0001$, $d_{av}= 2.6$, $\Delta=71.8\%$) and retention ($p< 0.001$, $d_{av}= 4.2$, $\Delta=95.06\%$; $p< 0.001$, $d_{av}= 2.2$, $\Delta=55.3\%$) in the VR + a-tDCS and VR + s-tDCS groups, respectively, compared to the control group. The **BC** was also significantly higher in the VR + a-tDCS group compared to the VR + s-tDCS group ($p< 0.001$, $d_{av}= 2.3$, $\Delta=45.7\%$) at the retention; **Fig. 2***(B)*.

**Table 2** Mean values of the Eye-Hand and Bimanual Coordination test score in three groups at Baseline, after the intervention and follow-up (Mean ± SD)

| Variable | Measurement | Groups | | |
|---|---|---|---|---|
| | | VR + a-tDCS | VR + s-tDCS | Control |
| EHC | Baseline | 0.43 ± 0.20 | 0.47 ± 0.25 | 0.46 ± 0.31 |
| | Post-intervention | 1.83 ± 0.43 $^{*,\&}$ | 1.45 ± 0.35 $^{*,\&}$ | 0.58 ± 0.34 |
| | Retention | 1.98 ± 0.39 $^{*,\&,\$}$ | 1.51 ± 0.48 $^{*,\&}$ | 0.62 ± 0.31 |
| BC | Baseline | 0.89 ± 0.17 | 0.82 ± 0.26 | 0.71 ± 0.27 |
| | Post-intervention | 1.91 ± 0.43 $^{*,\&}$ | 1.74 ± 0.43 $^{*,\&}$ | 0.82 ± 0.25 |
| | Retention | 2.39 ± 0.42 $^{*,\&,\$,\#}$ | 1.50 ± 0.36 $^{*,\&}$ | 0.85 ± 0.25 |

VR + a-tDCS = virtual reality and anodal Transcranial Direct Current Stimulation; VR + s-tDCS = virtual reality and sham Transcranial Direct Current Stimulation; EHC = eye-hand coordination; BC = bimanual coordination. $^*$ = significantly different from baseline withing the same group (all $ps<0.001$); $^\#$ = significantly different from post-intervention withing the same group ($p=0.008$); $^\&$ = significantly different from control at the same timepoint (all $ps<0.001$); $^\$$ = significantly different from VR + s-tDCS at the same timepoint (all $ps < 0.03$)

## Discussion

This study assessed the effect of a-tDCS$_{\text{UHCDS}}$ targeting both M1 and left DLPFC regions in addition to VR sports games on motor coordination of sedentary adolescent girls. Our findings provided more support for the efficacy of VR sports games in improving coordination skills as the EHC and BC were significantly higher in VR + a-tDCS$_{\text{UHCDS}}$ and VR + sh-tDCS groups compared to the control group at post-intervention and retention test. Moreover, as a novel finding, we observed that adding the a-tDCS$_{\text{UHCDS}}$ to the VR protocol resulted in higher improvement in EHC and BC compared to the sham condition at retention.

Our results showed that the VR + a-tDCS$_{\text{UHCDS}}$ and VR + sh-tDCS groups outperformed the control group in both coordination tasks (EHC and BC). Hence, we could assume that VR games used in the present study were able to improve coordination skills (when controlling the effects of a-tDCS$_{\text{UHCDS}}$) in sedentary adolescent girls, which is in line with the results of previous studies [20, 26, 27, 72–74]. Preliminary evidence supports this type of game as an enjoyable medium for low to moderate-intensity PA [75]. Providing accessible and attractive options for PA at home might overcome many of the reported barriers to PA, particularly for high-risk disability groups [76]. VR has been shown to increase motor coordination accuracy by improving visual feedback [18, 21]. These games can develop visual, auditory, and tactile inputs to improve coordination through repetition and practice, and provide feedback and motivation [19]. Given that

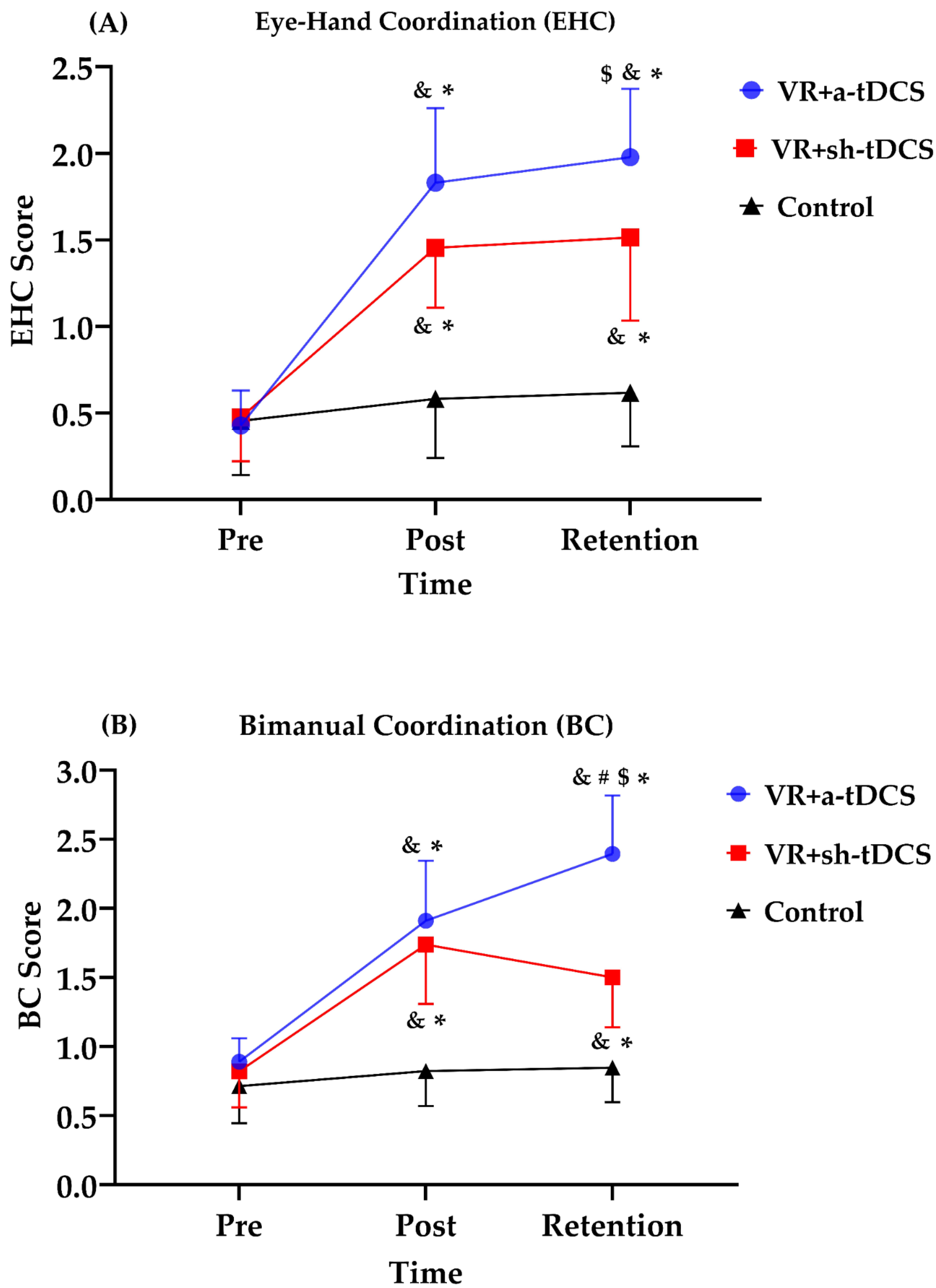


**Fig. 2** Mean values of the eye-hand coordination (**A**) and bimanual coordination test (**B**) in three experimental groups at the specified time points. VR + a-tDCS = virtual reality and anodal Transcranial Direct Current Stimulation; VR + s-tDCS = virtual reality and sham Transcranial Direct Current Stimulation. * = significantly different from baseline withing the same group (all *ps<0.001*); # = significantly different from post-intervention withing the same group ($p = 0.008$); & = significantly different from control at the same timepoint (all *ps<0.001*); $ = significantly different from VR + s-tDCS at the same timepoint (all *ps < 0.03*)

such games involve controlling each hand separately, an improvement in coordination is not far-fetched [20]. In addition, due to the use of Kinect in the VR games, participants had to use their whole body to continue playing and interacting with the graphical environment, which could also be an effective factor in improving motor coordination in sedentary adolescent girls after VR intervention without anodal brain stimulation. In fact, given the distance between the participants and the screen, they should use visual-spatial skills, bimanual coordination, eye-hand coordination, and shorter reaction time to control and execute the game properly [77]. According to the observational learning theory, learning motor skills from observation occurs through an input-output cognitive model, in which attention, retention, motor reproduction, and motivation are four processes that account for learning from observation [78]. It seems that this model can somehow explain the underlying mechanisms by which VR games can positively affect coordination skills. During the VR games, the participants would receive visual feedback from the screen and regulate it via the attentional process. This information could be stored for memory representation via the retention process, and then be converted into actions that resemble the modeled behavior via the reproduction process [78–80]. Finally, whether or not these behaviors become overt actions is determined by motivational processes [78].

On the other hand, the present study showed that the VR+a-tDCS$_{UHCDS}$ group outperformed the VR+sh-tDCS group in EHC and BC at the retention test (2 weeks after the end of interventions). Previous studies have paved the way for investigating the potential synergistic effects between tDCS and other intervention strategies in healthy and clinical populations [53, 81, 82]. Our results are in line with previous studies showing positive effects of tDCS on motor function and coordination [13, 83–85]. The DLPFC at the top of the motor hierarchy and the M1 at the bottom play an important role in the learning and performance of motor skills [15, 31, 43]. Interestingly, neuroplastic changes from higher-order areas (i.e. DLPFC) to lower-order areas (i.e. M1) are essential for procedural motor learning [86]. It seems that the tDCS montage used in the present study was able to induce favorable changes in the DLPFC and M1 areas leading to improvement in coordination skills. This could be attributed to the enhanced spatial coordinate system and motor coordinate system, which correspond to the main function of the DLPFC and M1, respectively [86]. In addition, one of the novel aspects of the present study was that tDCS was applied in each session before the VR games were performed. It should be noted that most previous studies have used a single tDCS session, whereas in our study we applied 12 a-tDCS$_{UHCDS}$ sessions on the same days as the VR games. The application of repeated sessions of tDCS is thought to have a cumulative effect that promotes/regulates the efficiency of information processing in neural circuits, leading to the synthesis of several proteins and subsequently to long-term-like potentiation (LTP) [87]. In other words, increasing excitability during successive tDCS sessions increases the chances of stronger and more effective synaptic communication between neurons activated during motor skill learning.

According to the literature, when it comes to synergistic effects between two or more interventions, the key factor is whether or not these interventions activate common mechanistic pathways [82]. We believe that the tDCS montage [simultaneous stimulation of DLPFC and M1 (dual-site tDCS)] and its repetitive nature (applied at each session before the VR games) were able to induce synergistic effects with the VR games, leading to greater outcome measures (higher EHC and BC) compared to the sham condition. Neuroimaging and fMRI studies have shown the involvement of DLPFC and M1 areas during exposure to VR games [88, 89]. Therefore, it seems that the tDCS montage used in the present study had a so-called pre-conditioning effect on the subsequent neural activities in the target brain areas triggered by the VR games. Such activation of shared neural circuits is likely to have provoked synergistic effects between tDCS and VR, culminating in additional benefits as seen in the higher motor coordination in the VR+a-tDCS$_{UHCDS}$ group compared to the VR+s-tDCS group. Jo et al. [90] provided further support for this claim by suggesting that the application of tDCS before training may be optimal for improving motor skill learning.

On the other hand, the results of the present study were not consistent with other previous studies that showed no effect of tDCS on motor skills [91–93]. The number of tDCS sessions may be one of the explanations for the divergent outcomes, because other studies used just one [91, 93] or four [92] tDCS sessions, while in this investigation 12 stimulation sessions were used. Therefore, the number of sessions may be one of the most important reasons for the efficacy of tDCS. Other reasons could be due to the duration of stimulation, since they used tDCS for 15 min [91, 93], while we applied tDCS for 20 min. In addition, the tDCS in this study was delivered offline (i.e., not during the VR exercises). In other studies, however, the stimulation was delivered online and at the same time as the exercises. Other possible reasons for the inconsistency between our results and previous studies could be related to stimulation intensity and electrode placement. In the studies by Furuya et al. [91] and McCambridge et al. [93], the stimulation intensity was 1 mA and the anode electrode was placed over the C3 or C4 areas, whereas in the present study, we used an intensity of 2 mA at each site to targeting to stimulate the DLPFC and M1 areas simultaneously.

Although all the necessary details were taken into account to ensure optimal control of the study procedure, the results of the present study must be interpreted with caution, as they are not free from the effects of limiting factors. Only inactive adolescent girls were included in this study, which limits the generalizability of the results to other populations. In addition, we were not able to include measures of brain activity (e.g., EEG, fNIRS, fMRI), corticocortical, corticospinal, and/or motor neuronal excitability, which would provide some direct insights into the possible mechanisms involved in the effects of tDCS and VR. Researchers should take these limitations into account when designing future studies. On the other hand, the strength of the present study includes the fact that we used repeated sessions of tDCS, whereas most of the tDCS literature is based on the effects of a single session. Furthermore, the fact that we used a novel dual-site tDCS montage in the motor learning/control area, targeting both M1 and the left DLPFC, could be considered a novel contribution of the present study, as these brain areas are important for motor learning/control. Finally, the combination of tDCS and VR training to assess possible synergistic effects could also be considered a novel contribution of the present study.

## Conclusion

The present results suggest that the application of the uni-hemispheric concurrent dual-site anodal tDCS protocol simultaneously targeting M1 and left DLPFC over 12 sessions can increase the effectiveness of VR training and improve performance in motor coordination tasks, namely eye-hand and bimanual coordination in sedentary adolescent girls. Therefore, from a practical point of view, this intervention protocol (VR+a-tDCS$_{UHCDS}$) could be considered effective in providing additional improvement in coordination skills. Our results may have practical implications for other healthy and clinical populations, so future studies are suggested to measure the efficacy of this intervention protocol in other target populations. Also, investigating the effectiveness of this intervention protocol on other motor functions could be another direction for future studies.

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**Author contributions**
NSH, AH, EA, and DM conceptualized and designed the study. NSH, AH, and EA conducted the experiments. NSH, AH, EA, and DM participated in the formal analysis. NSH wrote the original draft of the manuscript. AH, EA, and DM reviewed and edited the manuscript. All authors approved the final version of the manuscript.

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**Data availability**
No datasets were generated or analysed during the current study.

## Declarations

**Ethics approval and consent to participate**
Ethics approval and consent to participate This study was approved by the Ethics Committee of Razi University *(IR.RAZI.REC.1401.058)* and registered in the Iranian Registry of Clinical Trials *(IRCT id: IRCT20221124056598N1; Registration Date: 10-12-2022)*. All the experimental procedures were conducted following the declaration of Helsinki. Informed consent was obtained from all subjects before participation in the study.

**Consent for publication**
Not Applicable.

**Competing interests**
The authors declare no competing interests.

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