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Pushing athletic performance boundaries with anodal transcranial direct current stimulation: an exploratory, pilot, randomized controlled study on strength and inflammation in elite weightlifters

Renato de Donato[1], Marco Prenassi[2,3], Matteo Guidetti[4], Clara Tambussi[4], Roberta Ferrucci[4,5,6,7], Alessandra Vezzoli[8], Cinzia Dellanoce[8], Stefano Pastore[3], Alessandro Brunello[9^], Alberto Priori[4,6], Sara Marceglia[3,4*] and Simona Mrakic-Sposta[8]

Abstract

Background Transcranial direct current stimulation (tDCS) has been proposed as a non-invasive neuromodulatory strategy to enhance motor performance and modulate inflammatory responses. However, its effects on strength capacity and physiological stress markers during complex resistance exercises in elite athletes remain underexplored.

Methods In this exploratory, randomized, sham-controlled pilot study, ten elite male weightlifters ($n = 10$; active tDCS = 5, sham = 5) received either a single 20-min session of anodal tDCS (2 mA) over the motor cortex or sham stimulation immediately before performing high-load back squats (85% 1RM). Outcomes included repetition number, barbell kinematics, Borg Rating of Perceived Exertion (Borg-RPE), Visual Analogue Scale (VAS) measures, and metabolic and oxy-inflammatory biomarkers (blood glucose, lactate, antioxidant capacity; salivary ROS; urinary IL-6, 8-iso-PGF2α, 8-OH-dG, creatinine, and neopterin). Given the exploratory design and small sample size, intervention effects were analyzed using Mann–Whitney U tests. For outcomes assessed both before and after stimulation, between-group comparisons were performed on change scores (Δ = post − pre). In contrast, mechanical exercise-related variables, which were only collected after stimulation, were directly compared between the active and sham groups.

Results Athletes receiving active tDCS performed a significantly higher number of back squat repetitions and exhibited shorter lift times compared with the sham group ($p = 0.024$ and $p = 0.011$, respectively). No significant between-group differences were observed in Borg-RPE, VAS-based subjective measures, or biochemical markers (all $p > 0.05$). No significant differences were found for the remaining mechanical parameters (all $p > 0.05$).

[†]In memory of Alessandro Brunello.

*Correspondence:
Sara Marceglia
smarceglia@units.it

Full list of author information is available at the end of the article

Conclusions A single session of anodal tDCS applied before high-load back squat exercise may be associated with improvements in repetition capacity and lifting efficiency in elite weightlifters. No significant effects were observed on perceived exertion, biomechanical stability measures, or metabolic, oxidative, inflammatory, and renal biomarkers. These preliminary findings suggest that tDCS may represent a promising neuromodulatory adjunct to strength training, warranting confirmation in larger and methodologically powered studies.

Trial registration None (pilot study).

Keywords Non-invasive brain stimulation, Oxidative stress, Inflammation, Transcranial direct current stimulation, Back squat, Athletes, Strength and conditioning

Background

Muscular strength is a complex and multifaceted construct [1] that encompasses both neurophysiological [2] and psychological factors [3]. In weightlifting, a discipline where performance is centered on achieving maximal force output in compound movements such as the squat, bench press, and deadlift, athletes are trained to progressively increase their one-repetition maximum (1RM) in multi-joint exercises [4]. This process demands a comprehensive approach that encompasses musculoskeletal components like motor control, inter- and intra-muscular coordination, lifting technique, and psychological dimensions like emotion regulation, motivation, and attentional control [5]. Accordingly, weightlifting training can be conceptualized as a means to express the maximum strength possible, prompting the exploration of novel training strategies and tools. Within this performance context, exercise-induced imbalances in oxidative stress and inflammation have also been recognized as relevant physiological concerns, given their interdependence and potential for long-term detrimental effects [6, 7]. An increase in oxidative stress (OxS) has been observed following both aerobic and anaerobic exercise of sufficient intensity [8, 9], with the magnitude of the response being dependent on exercise type, duration, and load [10, 11]. OxS arises from an imbalance between reactive oxygen species (ROS) and the body's antioxidant defense systems. Numerous studies have demonstrated that acute exercise leads to elevated ROS production [12–14], thereby intensifying oxidative pressure on cellular structures [15, 16]. When excessive, this stress may impair physical performance and hinder skeletal muscle recovery [17] by altering contractile and regulatory proteins and disrupting calcium handling [18]. These alterations result in reduced force production and increased fatigue, particularly at submaximal intensities [18]. Excessive ROS may impair mitochondrial efficiency through damage to respiratory chain components and membrane lipids [11]. This phenomenon manifests as higher oxygen consumption at a given workload, shorter time to exhaustion, and greater perceived exertion in closely repeated sessions [19]. Moreover, muscle damage has been associated with post-exercise elevations in interleukin-6, a response with practical implications for recovery and subsequent performance [20]. Considering these mechanisms, quantifying biomarkers of oxidative stress and inflammation is essential, including ROS, 8-iso PGF2α, 8-OH-dG, and IL-6, which reflect oxidative cascades, lipid peroxidation, DNA damage, and muscle inflammation, respectively.

Alongside these biochemical considerations, transcranial direct current stimulation (tDCS) has shown promising results as a non-invasive neuromodulation technique in sports neuroscience to enhance sport performance [21]. tDCS involves the application of low-intensity direct current to the scalp to modulate cortical excitability [22]. Typically, anodal stimulation (atDCS) increases excitability, while cathodal stimulation (ctDCS) decreases it [23]. In particular, one of the most used electrode placements in tDCS involves an active electrode over the brain region of interest (e.g., motor cortex, M1) and a reference electrode often over a distant anatomical area (i.e., extracranial, such as the shoulder or deltoid) to complete the electrical circuit [24]. This approach has demonstrated the ability to make the stimulation more focused on the target area, avoiding "unwanted" effects due to the proximity of the electrical fields and possibly affecting subcortical circuits [24]. Emerging evidence suggests that tDCS may influence neuroinflammatory processes by modulating microglial activation and cytokine expression, potentially reducing pro-inflammatory markers in both preclinical and clinical models [25–30]. It should be noted that the inflammatory processes described in neurological disorders differ substantially from the transient systemic inflammatory responses induced by high-intensity exercise. In the context of resistance exercise, inflammatory signaling is primarily driven by peripheral muscle stress and metabolic perturbations rather than by central neuroinflammatory mechanisms [31]. Although tDCS is primarily known for modulating cortical excitability [32], changes in central motor drive, perception of effort, and autonomic regulation may indirectly interact with systemic physiological responses during intense exercise [33]. Through these central mechanisms, tDCS could potentially influence performance outcomes while interacting with metabolic and inflammatory processes

associated with strenuous muscular activity. In the sports domain, despite heterogeneity in protocols and populations studied, increasing evidence supports the use of atDCS over the M1 to improve endurance, power performance, and explosive force in various disciplines such as cycling and ski jumping [34, 35]. Additional studies have shown that atDCS can enhance muscle strength [36, 37], improve cognitive function [38], and reduce both central and peripheral fatigue [34] and pain perception [39]. However, most investigations on tDCS and muscular performance have focused on time to exhaustion during isolated and simple tasks, such as elbow flexion [37, 40], often overlooking more ecologically valid performance conditions that integrate cognitive, emotional, and motivational demands [40] – e.g., sport-specific [41], high-load conditions [42].

To date, few studies have examined the effects of tDCS on complex multi-joint strength performance while simultaneously assessing performance outcomes together with physiological responses in elite athletes. In the present study, we explored the impact of monopolar atDCS applied bilaterally over the M1, compared to sham stimulation, on athletic performance during high-load back squat (BS) exercises in elite male weightlifters, with a specific focus on the physio-biological effects of the intervention in terms of metabolic (glucose, lactate), oxidative-inflammatory (ROS, total antioxidant capacity, lipid peroxidation, DNA oxidation, IL-6), and renal biomarkers (creatinine, neopterin). The results are intended to inform future studies aimed at investigating the effects of neurostimulation targeting motor regions on performance, as well as on inflammatory and neurobiological profiles.

Methods

Study design and setting

In this prospective, sham-controlled, exploratory pilot clinical study, 10 elite weightlifting athletes were randomly assigned to either an active anodal tDCS group (active tDCS, n = 5) or a sham stimulation group (sham tDCS, n = 5) (Fig. 1). Each participant, blinded to the treatment group, received a single 20-minute session of tDCS (active or sham) immediately prior to performing a high-load BS exercise. Performance was evaluated by measuring the total number of BS repetitions completed, alongside a set of biomechanical parameters, including gyroscope-based oscillation analysis, angular momentum energy estimation, oscillation count during the lift phase, and horizontal sway as tracked by a motion capture camera. Subjective perceptions of effort and well-being were assessed using the Borg Rating of Perceived Exertion (Borg-RPE) and a Visual Analogue Scale (VAS), respectively. Additionally, physiological responses were assessed through blood, saliva, and urine biomarkers, collected at two timepoints: immediately before (T0, throughout the text referred to as "pre") and after (T1, throughout the text referred to as "post") the BS exercise. Assessors were not blinded to participant allocation. This study was designed as an exploratory pilot trial aimed at assessing feasibility and estimating preliminary effect

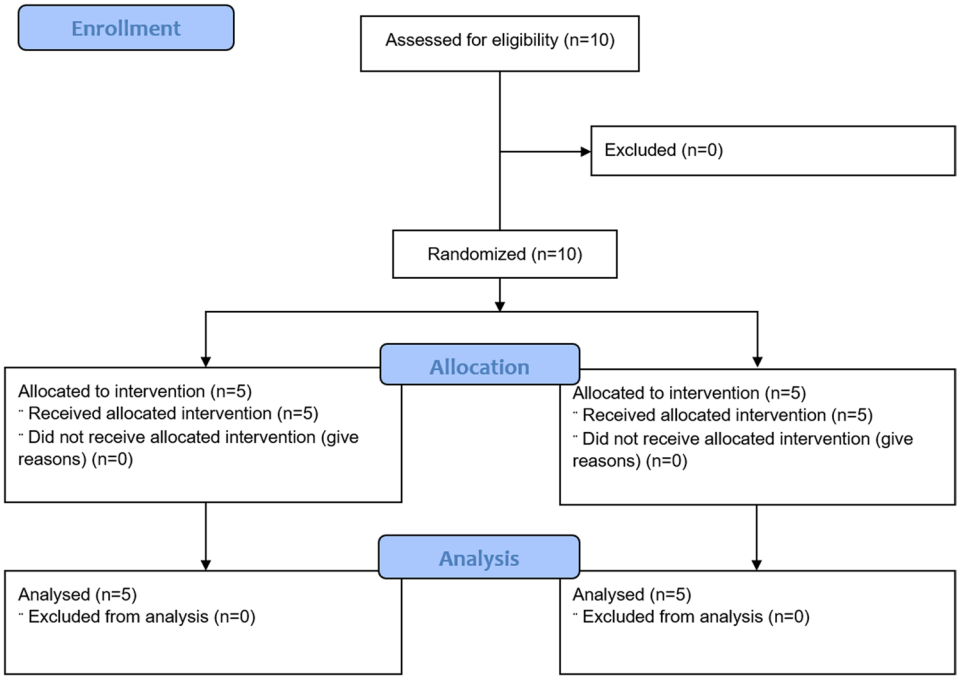

Fig. 1 Flowchart diagram depicting the flow of participants through the study

sizes rather than providing confirmatory hypothesis testing. Given the limited sample size, statistical analyses were considered exploratory, and p-values were interpreted descriptively rather than as confirmatory evidence of population-level effects. In this sense, analyses could inform future power calculations and lay the foundations for further, powered and more methodologically solid studies. All procedures were conducted in accordance with the Declaration of Helsinki and were approved by the Ethics Committee of the IRCCS Ca' Granda Foundation—Maggiore Policlinico Hospital of Milan (approval number J274-2022). All subjects gave written informed consent before participation.

Participants

Participants were recruited via invitation from the Milan section of the Italian Weightlifting Federation (Federazione Italiana Pesistica – FIPE). Inclusion criteria were: (I) age ≥ 18 years; (II) official registration with FIPE as "expert" athletes in the "Senior" category across different weight classes [43]; (III) ability to understand and perform the study procedures; and (IV) capacity to provide written informed consent. Exclusion criteria included: (I) history or presence of major neurological, neuropsychological, or psychiatric disorders, as determined by clinical history; and (II) the presence of implanted medical devices such as pacemakers, intracranial metallic components, or spinal cord stimulators. To minimize potential confounding effects of prior physical exertion, all athletes were instructed to abstain from exercise for at least 24 h prior to the study session, following the guidance of a certified FIPE trainer (A.B.).

tDCS protocol

tDCS, either active or sham, was administered in a single session immediately prior to the BS exercise. Stimulation was delivered using a constant-current stimulator (HDCStim, Newronika, Italy) connected to silicone rubber electrodes (1 mm thickness) with an area of 35 cm^2 (7 × 5 cm) for the anodes and 48 cm^2 (8 × 6 cm) for the cathode. The anodal electrodes were positioned bilaterally over M1 (corresponding to C3 and C4 according to the international 10–20 EEG system), while the cathode was placed over the right deltoid muscle [24]. Indeed, as demonstrated in previous literature, this montage induces more focal and deeper stimulation [24]. Conductive gel was applied to ensure stable and low-impedance electrode–skin contact throughout the stimulation. For the active condition, direct current was applied at 2 mA for 20 min, with a 30-second ramp-up and ramp-down period. The resulting charge density (68.57 mC/cm^2) was within established safety limits [44, 45]. In the sham condition, the device delivered only the initial 30-second ramp-up followed by a ramp-down, mimicking the somatosensory sensations of active stimulation without inducing lasting neuromodulatory effects [46], thereby maintaining participant blinding [47]. To verify blinding, subjects were asked at the end of the session whether they thought to have received active or sham stimulation.

BS task

Participants were instructed to perform the maximum number of repetitions of the BS exercise with a barbell loaded at 85% of their 1RM, as assessed before the experiment. The exercise involved lowering the body with the barbell positioned on the upper back, between the seventh cervical vertebra and the scapular spine, until reaching a squat depth where the tops of the thighs were parallel to the floor ("parallel" position). Execution of the high-load BS required the athlete to control multiple performance-related variables, including barbell trajectory, joint angles at the knees and ankles, postural adjustments, foot positioning, and ground contact. This complex motor task allowed for the integration of both neuromuscular and subjective (cognitive-emotional) factors involved in strength execution. To prevent performance from being influenced by habitual training routines, the actual barbell load was concealed using opaque covers. This approach encouraged athletes to rely on perceived exertion rather than prior expectations about the load, thereby promoting a more authentic maximal-effort performance. Movement analysis focused on capturing barbell trajectory and detecting imbalances throughout the lift. A visual motion tracking system was used to assess lateral sway (Fig. 2), and to enhance motion analysis, inertial measurement units (IMUs) were affixed to the barbell to measure rotational dynamics along its central axis (Fig. 2). Further details on biomechanical outcome measures are provided in the biomechanical outcomes.

Clinical outcomes

Perceived exertion was assessed using the Borg Rating of Perceived Exertion (Borg-RPE), a 15-point scale that includes standardized verbal descriptors to quantify subjective effort, breathlessness, and fatigue across a range of physical tasks and individuals [48].

Subjective symptoms were further evaluated using a 10-centimeter Visual Analogue Scale (VAS), in which the left anchor (score = 0) represented the absence of a symptom, and the right anchor (score = 10) represented the most intense symptom imaginable [49]. Participants were asked to indicate the intensity of their perceived symptoms at the given moment by marking a point along the line. VAS assessments included mood, general wellness (e.g., happy/unhappy, rest/tired), general sensations (e.g., hot/cold, calm/agitated), and pain (with anatomical location specified).

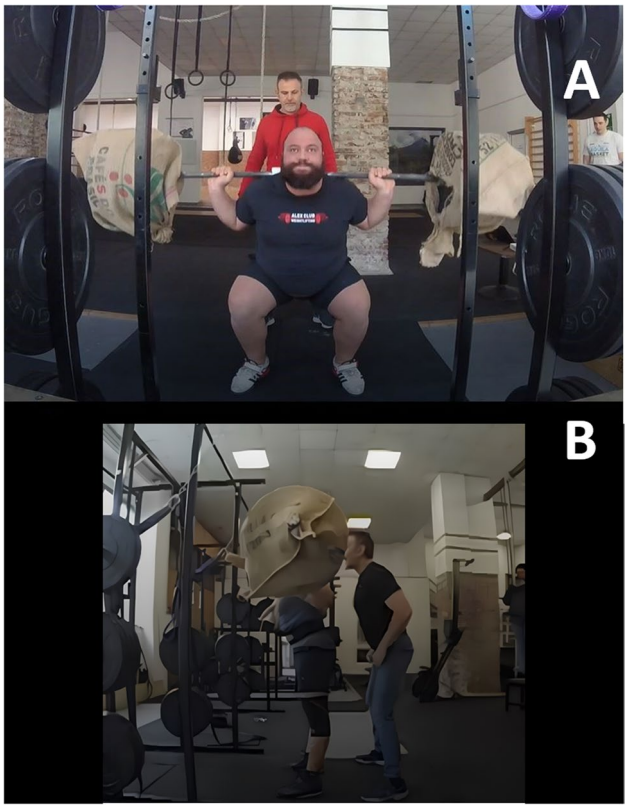

Fig. 2 Experiment setup and squat motion. **A**: Front view, **B**: Side view

Biochemical outcomes

Biochemical outcomes were obtained through capillary blood, saliva, and urine samples. Capillary blood was collected from a fingertip for the determination of blood lactate concentration, glycemia, and total antioxidant capacity (TAC). Saliva was collected in Salivette devices (Sarstedt, Nümbrecht, Germany). Urine samples were collected by voluntary voiding in a sterile container. All saliva and urine samples were stored in multiple aliquots at -20 °C until assayed and thawed only once before analysis, which was performed within two weeks of collection.

Metabolic markers

Blood lactate concentration ([La]b) was assessed using an enzymatic method (Lactate Scout 4; EKF Diagnostic for Life, Germany) with 0.2 µL of capillary blood collected from the fingertip. Blood glucose levels were measured using an electronic glucometer with Accu-Chek Active test strips (Roche Diagnostics) on a fingertip blood sample. Each test was conducted in duplicate for all participants [13].

ROS production, antioxidant capacity, and oxidative damage

ROS production rate was assessed in saliva by Electron Paramagnetic Resonance spectroscopy (EPR), operating X-band (E-Scan- Bruker BioSpin, GmbH, MA USA) as previously described [15, 50]. Sample temperatures were stabilized at 37 °C by a temperature controller ("Bio III" unit, Noxigen Science Transfer & Diagnostics GmbH, Germany), interfaced with E-Scan, and CMH spin trapping molecules (also referred to as probes), 1-hydroxy-3-methoxycarbonyl-2,2,5,5- tetramethylpyrrolidine (CMH, Noxygen Science Transfer & Diagnostics, Germany) were used. The EPR signal reflects the number of unpaired electrons and can be translated into absolute production rates (µmol·min^{-1}). The stable CP (3-Carboxy-2,2,5,5-tetramethyl-1-pyrrolidinyloxy) radical was measured independently and served as a reference standard. TAC was measured by a redox sensor using a commercial EDEL potentiostat electrochemical analyser (Edel Therapeutics, Switzerland) in a three-electrode arrangement, in 10 µL of capillary blood [51, 52].

Oxidative damage and inflammatory markers

The levels of 8-isoprostane (8-iso-PGF2α), 8-hydroxy-2'-deoxyguanosine (8-OH-dG), and interleukin-6 (IL-6) were determined in urine using ELISA assays (Enzyme-Linked Immunosorbent Assay). All determinations were carried out using a microplate reader spectrophotometer (InfiniteM200, Tecan, Austria). All the assessments were duplicated, and the interassay coefficient of variation was within the range indicated by the kit's manufacturer. Briefly, lipid peroxidation and DNA damage were assessed using commercial kits (Cayman Chemical, Ann Arbor, Michigan, USA, Item No. 516351 and Item No. 89320 respectively) as previously described [13, 53];

samples were read at a wavelength of 412 nm, and concentration were determined using standard curves as previously described. The coefficient of variation (CV) was indicated by the manufacturer: inter-assay CV 11.2% and 10.7% and intra-assay CV 14.6% and 11.6%, respectively, for 8-iso-PGF2α and 8-OH-dG [52]. IL-6 in urine (IL-6-U) was determined by Human IL- 6 Immunoassay (Fine Test, Wuhan, China, Cat No.: EH0201) as previously described [13, 53]. The samples' concentrations were determined at 450 nm. The CV was indicated by the manufacturer: inter-assay CV 4.62%, and intra-assay CV 5.35%;

urinary lipid peroxidation was assessed by competitive immunoassay of 8-iso-PGF2α (Cayman Chemical, USA) as previously described [13, 53]; 8-OH-dG was quantified using a commercially available enzyme-linked immunosorbent assay (EIA) kit (Cayman Chemical, Ann Arbor, MI, USA, Item No.589320). The sample 8-OH-dG concentration was determined using a standard curve as previously described [52]. Neopterin concentrations were measured in duplicate using an isocratic high-pressure liquid chromatography (HPLC) method. The calibration curves were linear for creatinine (1.25–10 mmol/L), and

neopterin (0.125–1 µmol/L). The inter-assay and intra-assay variation coefficients were below 5%. The methods have been previously described [52].

Renal function

Bilirubin, urobilinogen, ketones, blood proteins, pH, and leukocytes, as well as specific gravity/density, were assessed semi-quantitatively using Urine Test Strips (Combi screen 11sys PLUS, GIMA, Gessate, Milan, Italy) in duplicate for each subject [13]. Creatinine assessment followed the one previously described for neopterin.

Biomechanical outcomes

Biomechanical variables and analyses were customized for this pilot study. Briefly, to quantify rotational instability of the barbell, we employed a differential signal analysis from the two IMUs units mounted on the barbell (Fig. 3). This allowed us to minimize structural deformation artifacts and isolate true instability in barbell rotation. As shown in Fig. 3, the difference between the two-sensor signal was calculated to attenuate the deformations of the barbell and to amplify the actual balancing act on the barbell to characterize the gesture of the athlete.

The signal was band-pass filtered (0.5–4 Hz) to remove noise related to gravity or high-frequency peaks. Within the concentric phase, two measures were computed: (I) the angular momentum energy, normalized to the weight lifted, to estimate the magnitude of oscillation; and (II) the number of oscillations during the lift phase, calculated via peak detection, as a proxy for motion regularity and control. The latter was particularly useful for identifying instability during the initial concentric stage. To count the number of oscillations, a simple peak detection algorithm was applied on the post-processed signal, using the total number of peaks detected as an oscillation estimate (Fig. 4).

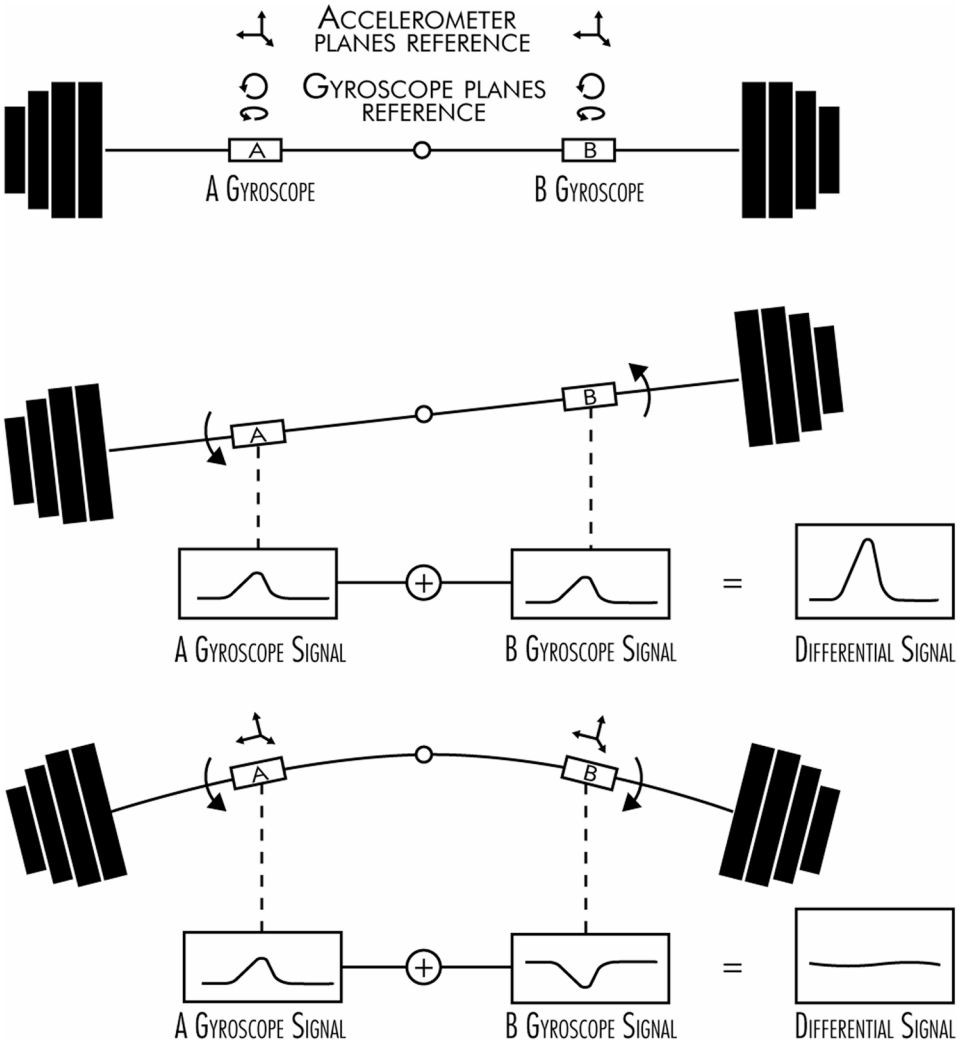

Fig. 3 Gyroscope sensor position on the barbell and signal deformation attenuation using the differential of the two recording units

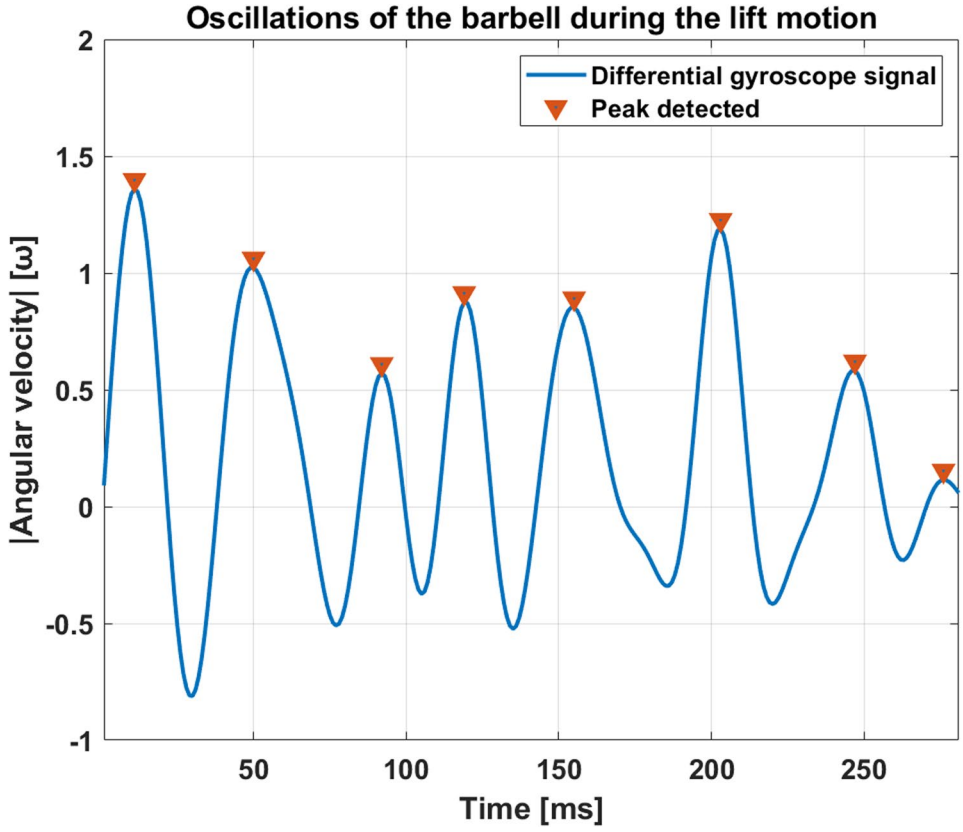

Fig. 4 Peak detection algorithm applied to the post-processed differential module of the two barbell gyroscopes in the subject 1, during the first lift phase. In this example there are 8 oscillations

In addition, the horizontal sway of the barbell was assessed from the x-axis displacement in the lateral video recordings. This metric was normalized to each athlete's lifted weight. Since all athletes started from the same position and camera setup remained fixed, we used pixel displacement in the vertical (y) axis as a consistent reference. To extract the sway feature we calculated the maximum extensions of the horizontal offset during each single phase (Fig. 5). These measurements were made for all the repetitions during the exercise of the athletes. To better account for the effects of fatigue on motor control, repetitions were further classified based on their velocity. For each athlete, the mean duration of the eccentric–concentric cycle was used as a threshold. Repetitions faster than the mean were labeled as "fast" (typically occurring at the beginning of the set), while slower repetitions (generally appearing later as fatigue accumulated) were categorized as "slow." This classification allowed us to explore changes in movement quality across the course of the task.

Statistical analysis

Data distribution was assessed using the Shapiro–Wilk test. Given the small sample size ($n = 5$ per group) and violations of normality in several variables, non-parametric tests were adopted throughout the analysis. Between-group comparisons were performed using Mann–Whitney U tests, with effect size expressed as rank-biserial correlation where applicable. For variables assessed both before and after stimulation, including clinical outcomes, biochemical outcomes, and total repetition number, between-group comparisons were conducted on change scores ($\Delta = \text{post} - \text{pre}$) to account for baseline interindividual variability. For the remaining mechanical exercise-related variables, comparisons were performed on post-stimulation values only (Active vs. Sham), because the maximal exercise task could not be repeated before and after stimulation. Descriptive statistics are reported as mean ± standard deviation (SD). Statistical significance was set at $p < 0.05$ (two-tailed). All statistical analyses were performed using Jamovi (version 2.6).

Results

Ten male weightlifting athletes were included (age 27.3 ± 5.27 years). All of them were expert weightlifters based on training history (6.0 ± 5.5 years) and high relative load performance (~ 85% 1RM; 174.05 ± 22.28 kg). Demographic and anthropometric characteristics of the sample are summarized in Table 1. Anthropometric

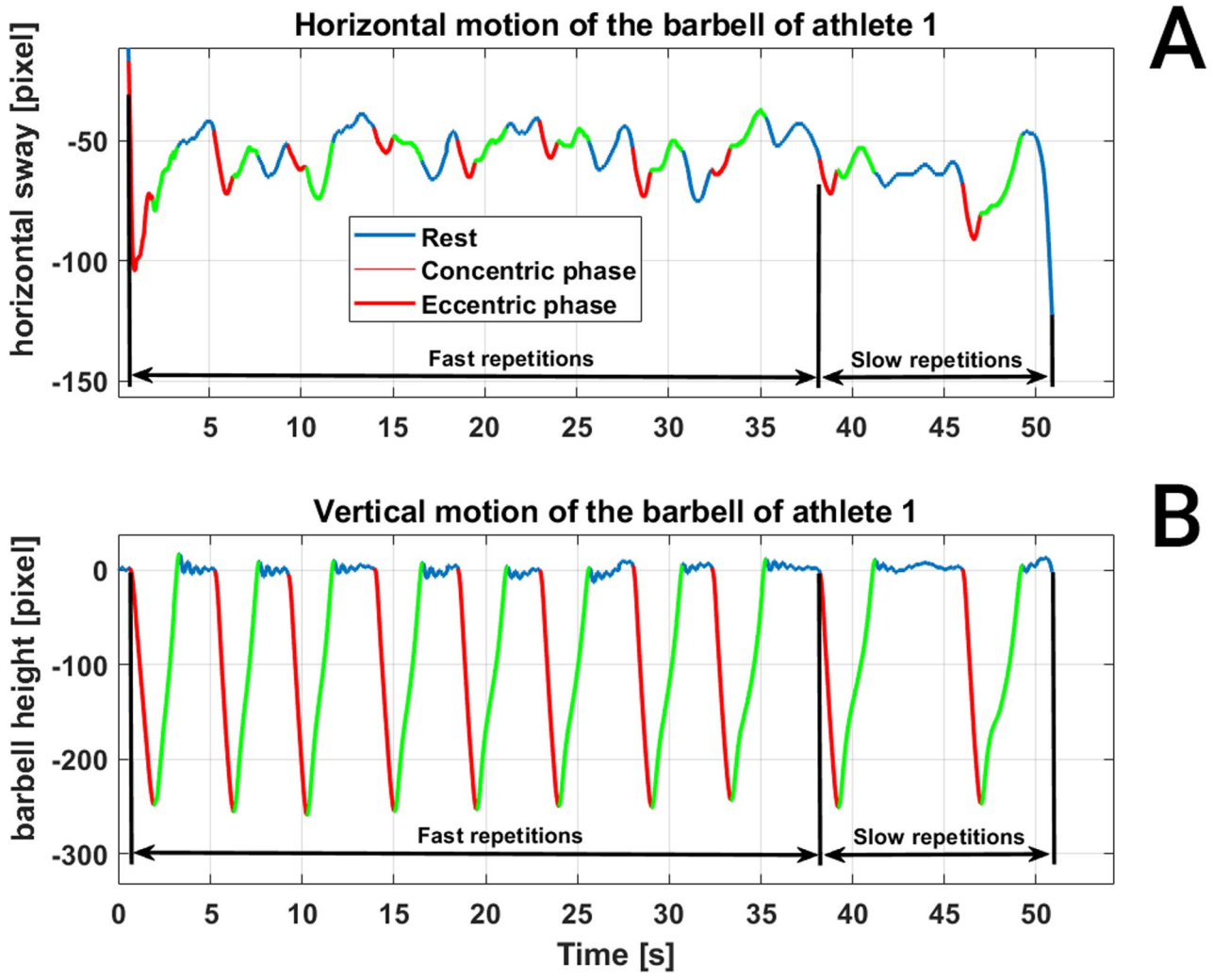

Fig. 5 Camera tracking trajectory sway segmentation and fast/slow repetitions segmentation example, (**A**) Horizontal camera tracked barbell motion, (**B**) Vertical camera tracked barbell motion

parameters were obtained using bipolar bioelectrical impedance analysis (TBF-300 A Body Composition Analyzer; Tanita Corporation, Arlington Heights, IL, USA), a method that may present some limitations in the assessment of body composition [54]. All participants were in good health and reported no history of smoking. Additionally, the training history of each athlete was recorded to better contextualize individual performance profiles. When participants were asked to identify their treatment condition in order to assess the success of blinding, they were unable to determine which study arm they had been assigned to.

Descriptive statistics, together with Mann–Whitney U test results, are reported in Table 2. The table specifies whether each comparison was conducted on change scores ($\Delta = \text{post} - \text{pre}$) or on post-stimulation values only. No significant differences were observed between the active tDCS and sham groups for perceived exertion (Borg-RPE) or for any VAS dimension, including well-being, tiredness, heat, restlessness, happiness, and pain (all $p > 0.05$). For the mechanical exercise-related variables (total repetitions, lift time, fast repetitions, slow repetitions, angular momentum energy, rotational oscillations in the concentric phase, and normalized horizontal sway), significant between-group differences were detected for total repetitions ($p = 0.024$) and lift time ($p = 0.011$), whereas no significant differences were observed for the remaining mechanical variables (all $p > 0.05$). Similarly, no significant between-group differences were observed for blood glucose, blood lactate, ROS production, total antioxidant capacity, 8-iso-PGF2α, 8-OH-dG, urinary IL-6, creatinine, neopterin, bilirubin, urobilinogen, ketones, erythrocytes, urinary pH, leukocytes, or specific gravity (for all, $p > 0.05$).

Table 1 Demographic and anthropometric characteristics of the sample, divided by group

Subject	Age	Kg	Height	Body fat	FFM	TBW	PMM	BMI	Repetitions number Basal assessment	Weights [kg] (85% of maximum)	Repetition number Experiment	How much do you think you have lifted?	Borg Scale
Active tDCS Group													
1	26	144.8	177	40.9	85.5	62.4	81.3	46.22	5	178.5	10	190	13
2	36	94.8	190	14.5	80.2	57.6	76.3	26.26	9	161.5	11	160	19
4	21	88.7	184	12.7	76	59.2	72.2	26.2	7	135	8	135	16
7	22	76.4	165	11.8	64.6	60.2	61.8	28.06	5	210	7	205	19
8	34	108.4	190	14.7	93.7	58.6	89.1	30.03	5	187	7	180	17
mean	27.8	102.62	181.2	22.6	80	56.16	76.14	31.354	6.2	174.4	8.6	174	16.8
SD	6.87	26.24	10.52	20.55	10.85	6.20	10.20	8.46	1.78	28.11	1.81	27.24	2.49
Sham tDCS Group													
3	24	116.4	191	20.8	95.6	57	90.9	31.91	6	178.5	7	170	16
5	27	80.3	175	8.6	71.7	62	68.1	26.22	5	150	6	145	17
6	31	88.8	168	21.4	67.4	54.4	64.1	31.46	6	170	7	170	19
9	30	86.8	172	18.3	68.5	55.5	65.1	29.34	5	170	6	170	18
10	22	84.6	175	11.5	73.1	60.5	69.5	27.62	5	200	5	200	19
mean	26.8	91.38	176.2	16.12	75.26	57.88	71.54	29.31	5.4	173.7	6.2	171	17.8
SD	3.834	14.34	8.76	5.75	11.60	3.26	11.04	2.44	0.55	18.05	0.84	19.5	1.30

FFM Fat-Free Mass, *TBW* Total Body Water, *PMM* Predicted Muscle Mass, *BMI* Body Mass Index

Table 2 Summary of the outcomes considered in the study

Variable	Comparison metric	Active tDCS (mean ± SD)	Sham tDCS (mean ± SD)	U	*p*-value	Rank-biserial *r*
Clinical						
Borg-RPE (perceived exertion)	Δ (post – pre)	16.80 ± 2.48	17.80 ± 1.30		> 0.05	
VAS well-being	Δ (post – pre)	3.06 ± 1.79	3.9 ± 1.62		> 0.05	
VAS tiredness	Δ (post – pre)	4.5 ± 1.26	6.94 ± 1.76		> 0.05	
VAS heat	Δ (post – pre)	1.64 ± 2.22	1.76 ± 1.12		> 0.05	
VAS restlessness	Δ (post – pre)	5.14 ± 2.70	3.62 ± 2.57		> 0.05	
VAS happiness	Δ (post – pre)	1.6 ± 0.90	2 ± 0		> 0.05	
VAS pain	Δ (post – pre)	2.2 ± 2.70	1 ± 1		> 0.05	
Mechanical						
Total repetitions (n)	Δ (post – pre)	2.40 ± 1.52	0.80 ± 0.45	2.00	**0.024***	−0.840
Fast repetitions (n)	Post only	2.2 ± 0.4	2.6 ± 0.49		> 0.05	
Slow repetitions (n)	Post only	3 ± 0.63	5 ± 1.79		> 0.05	
Angular momentum energy (°s^(-1) Hz^(-0.5))	Post only	0.0048 ± 0.0071	0.0201 ± 0.0245		> 0.05	
Rotational oscillations in concentric phase (n)	Post only	10.53 ± 2.89	12.44 ± 3.64		> 0.05	
Lift time (sec)	Post only	1.66 ± 0.08	1.97 ± 0.12	1.00	**0.011***	+ 0.920
Normalized horizontal sway	Post only	0.363 ± 0.175	0.435 ± 0.225		> 0.05	
Biochemical						
Blood glucose (mg/dL)	Δ (post – pre)	92.67 ± 10.79	81.75 ± 12.97		> 0.05	
Blood lactate ([La]b(mM))	Δ (post – pre)	9.26 ± 2.45	12.54 ± 2.82		> 0.05	
ROS production (µmol·min-1)	Δ (post – pre)	0.19 ± 0.01	0.20 ± 0.01		> 0.05	
Antioxidant capacity (TAC) (mM)	Δ (post – pre)	3.25 ± 0.13	3.42 ± 0.25		> 0.05	
8-iso-PGF2α (ng·mg-1 creatinine)	Δ (post – pre)	0.72 ± 0.40	0.73 ± 0.21		> 0.05	
8-OH-dG (ng/mL)	Δ (post – pre)	3.72 ± 1.11	4.81 ± 1.17		> 0.05	
Urinary IL-6 (pg. mL-1)	Δ (post – pre)	8.87 ± 3.30	7.64 ± 2.85		> 0.05	
Creatinine (g.L-1)	Δ (post – pre)	0.60 ± 0.10	0.66 ± 0.30		> 0.05	
Neopterin (µmol.mol-1creatinine)	Δ (post – pre)	277.60 ± 72.21	306.40 ± 108.20		> 0.05	
Bilirubin (µmol.L-1)	Δ (post – pre)	4.4 ± 2.5	3.2 ± 2.7		> 0.05	
Urobilinogen (µmol.L-1)	Δ (post – pre)	0.8 ± 0.7	0.3 ± 0.4		> 0.05	
Ketones (mmol.L-1)	Δ (post – pre)	4.0 ± 2.2	4.2 ± 3.2		> 0.05	
Erythrocytes (Ery.µL-1)	Δ (post – pre)	3.6 ± 4.9	5.4 ± 4.9		> 0.05	
pH	Δ (post – pre)	6.6 ± 0.9	6.2 ± 0.8		> 0.05	
Leukocytes (Leuko.µL-1)	Δ (post – pre)	3.0 ± 6.7	0.0 ± 0.0		> 0.05	
Specific gravity	Δ (post – pre)	1.02 ± 0.0	1.02 ± 0.0		> 0.05	

Values are reported as mean ± standard deviation

Between-group comparisons were performed using Mann–Whitney U tests

For variables assessed both before and after stimulation, including clinical outcomes, biochemical outcomes, and total repetitions, analyses were conducted on change scores (Δ = post – pre)

For the remaining mechanical exercise-related variables, analyses were conducted on post-stimulation values only, as the maximal exercise task could not be repeated before and after stimulation

Mann–Whitney U statistics and rank-biserial correlations are reported for statistically significant between-group comparisons

Statistically significant differences are indicated in bold and with an asterisk (*$p < 0.05$)

RPE Rating of Perceived Exertion, *VAS* Visual Analogue Scale, *ROS* Reactive Oxygen Species, *TAC* Total Antioxidant Capacity, *8-iso-PGF2α* 8-iso-Prostaglandin F2α, *8-OH-dG* 8-hydroxy-2′-deoxyguanosine, *IL-6* Interleukin-6, *pH* potential of Hydrogen

Discussion

In this randomized, sham-controlled, exploratory study, we explored the acute effects of atDCS on biomechanical, clinical, and biochemical responses during high-load BS performance in elite weightlifting athletes. Athletes who received active stimulation demonstrated a significant increase in the total number of repetitions, performed at a faster pace, compared to the sham group. No differential effect emerged between the fast- and slow-repetition subgroups, suggesting an overall improvement in task performance under the tested condition. These findings support the hypothesis that a single session of anodal tDCS may enhance both physical performance and motor control during high-intensity resistance exercise. However, despite the higher performance observed in the active stimulation group, no measurable

differences in perceived exertion or exercise-related oxidative/inflammatory biomarkers were detected in the present pilot sample, with potential implications for neuromodulatory strategies in elite training protocols.

To our knowledge, this is the first study to investigate the interaction between tDCS and repeated high-load BS using a multimodal assessment approach, including micro-invasive sampling of capillary blood, saliva, and urine to evaluate systemic oxy-inflammatory responses. This methodology allows for a more comprehensive characterization of physiological adaptations to acute neuromodulation in elite athletes, a population where physiological precision and training efficiency are critical [53, 55–57].

From a physical performance perspective, athletes who received active stimulation performed a higher number of repetitions with reduced lift time. While no significant differences emerged in fast repetitions, slow repetitions, angular momentum energy, rotational oscillations in the concentric phase, or normalized horizontal sway, the increased total performance supports the idea that tDCS can facilitate more efficient neuromuscular activation during complex strength tasks [58], even in the absence of overt changes in conventional biomechanical parameters. Previous research has demonstrated that anodal tDCS applied over the M1 can increase force generation, enhancing performance in maximal voluntary contraction tasks [59] and improving motor control [60–62]. These effects are thought to arise from increased corticospinal tract excitability [63, 64], ranging from cortical neuron activation [65] to motor unit recruitment [66], ultimately strengthening the descending drive from cortex to muscle and resulting in more efficient muscle activation [67]. In parallel, atDCS has been shown to promote more synchronized activation of agonist muscles and more effective inhibition of antagonist muscles [65]. Nonetheless, its effects on muscular endurance remain inconclusive [59]. Furthermore, tDCS may reduce perceived exertion [58, 68] and delay neuromuscular fatigue, thereby supporting performance gains in both endurance and strength domains [60–62]. Interestingly, our results occurred in absence of differences in between-group comparisons of perceived exertion (Borg-RPE). This suggests that, despite similar perceived effort, the active tDCS group achieved greater performance. These findings are consistent with a randomized controlled trial by Dos Santos et al. (2023), which demonstrated that motor anodal tDCS acutely improved 5,000 m running performance, yielding faster times and higher average velocity compared with sham, without changes in subjective RPE [69]. Such effects may arise because tDCS might acts primarily through increased neural excitability and motor unit recruitment rather than through sensory or cognitive pathways underlying the perception of effort [70].

Biochemically, no significant between-group differences emerged in metabolic markers (blood lactate and blood glucose), oxidative stress parameters (ROS production and TAC), inflammatory markers (8-iso-PGF2α, 8-OH-dG, IL-6), or indices of renal function (creatinine, bilirubin, urobilinogen, ketones, blood proteins, pH, leukocytes, and specific gravity/density). For most of these biomarkers, direct comparison with the existing literature is challenging, as no prior studies have specifically investigated these outcomes in relation to tDCS; therefore, conclusions can only be drawn indirectly from broader investigations. To date, no evidence has been reported regarding a potential direct effect of tDCS on renal function or on inflammatory biomarkers such as 8-iso-PGF2α and 8-OH-dG. However, a study conducted in healthy adults with obesity undergoing anodal tDCS applied to the dorsolateral prefrontal cortex for three consecutive mornings demonstrated a stimulation-induced reduction in plasma IL-6 concentrations compared with the sham condition [71]. These results are only partially comparable, given the differences in both population and stimulation protocol. Nevertheless, they provide useful insight into the potential biochemical effects of tDCS, considering that the significant increase in physical effort occurred with no significant increase in inflammatory response between groups. The available literature investigating the anti-inflammatory effects of stimulation through peripheral biomarkers has primarily focused on clinical populations rather than healthy individuals. For example, studies conducted in knee osteoarthritis [72] and stroke [73] have assessed inflammatory cytokines such as IL-6, TNF-α, and IL-10, although the results remain inconclusive. Similarly, the literature on tDCS and oxidative stress largely concerns clinical populations or animal models and suggests that tDCS may modulate oxidative stress pathways [25]. For instance, a randomized trial in stroke survivors demonstrated that tDCS combined with physiotherapy increased serum superoxide dismutase, an antioxidant enzyme involved in scavenging oxygen radicals [25]. In addition, Li et al. [74] showed that anodal tDCS applied over the frontal cortex of mice reduced levels of malondialdehyde, a key marker of lipid peroxidation [75], potentially through a tDCS-induced upregulation of brain-derived neurotrophic factor (BDNF), which is known to exert antioxidant effects [76].

In contrast, metabolic markers have been more extensively investigated. A crossover study showed that a single session of anodal tDCS promoted systemic glucose uptake and improved systemic glucose tolerance as measured with the euglycemic–hyperinsulinemic clamp [77]. A similar effect was observed when tDCS was applied twice in series [78]. In addition, in healthy subjects, stimulation resulted in blood glucose concentrations

that were distinctly lower under the tDCS condition compared with sham as early as day 1, with persistence of the effect at day 8 [79]. However, in all these studies the experimental conditions did not include any form of athletic performance or physical exertion, unlike in the present study. This warrants particular caution in making comparisons, as blood glucose is known to increase during exercise as a well-established acute physiological response to increased energy demand [80]. Regarding blood lactate, healthy individuals have been assessed primarily following sport-related efforts. In one study, anodal stimulation over the left dorsolateral prefrontal cortex increased time to exhaustion during cycling and, at exhaustion, was associated with significantly higher blood lactate accumulation compared with the sham condition [81]. Furthermore, a systematic review conducted in healthy adults concluded that, during cycling protocols, tDCS was associated in some studies with increased blood lactate accumulation, together with improvements in time to task failure and reductions in perceived exertion [82]. However, findings regarding lactate are not consistent. A 2024 triple-blind crossover study in recreational runners reported no differences between anodal tDCS and sham in blood lactate, nor in torque, motor-evoked potentials (MEP), or perceived exertion [83]. These observations suggest that, when lactate changes are observed, they may primarily reflect greater tolerance to effort or differences in task-related motor dynamics rather than a direct and robust effect of tDCS on the systemic regulation of lactate under resting conditions [82].

This study has several limitations. First, the small, unstratified, all-male sample size, although justified by the elite status of the athletes, limits statistical power and generalizability. In addition, the absence of blind assessors may have increased the risk of biased assessments. Second, the study examined only the acute effects of a single tDCS session, without assessing potential long-term or cumulative adaptations (e.g., tolerance or chronic adaptations), and lacked direct neurophysiological measures (e.g., motor-evoked potentials, EEG, TMS-derived metrics) to clarify the underlying cortical mechanisms. Third, potential confounding factors such as nutritional intake, sleep patterns, and circadian timing were not standardized, and the timing of biomarker assessment ("immediately post" exercise) may have missed peak fluctuations in IL-6 and oxidative stress responses.

Conclusion

This randomized, sham-controlled, exploratory study provides preliminary evidence that a single session of anodal tDCS, applied prior to high-load BS exercise, may enhance neuromuscular endurance and athletic performance, without detectable increases in the measured systemic oxidative and inflammatory biomarkers. In this small pilot sample, no significant between-group differences were detected in metabolic markers, oxidative stress parameters, inflammatory markers, or indices of renal function. These findings highlight the potential of tDCS as a neuromodulatory adjunct to conventional strength training, particularly in elite athletic settings. Future studies involving larger samples and repeated stimulation protocols are warranted to confirm these results and to investigate the long-term benefits and mechanisms of action of tDCS in strength-based sports.

Abbreviations

BS	Back squat
1RM	One-repetition maximum
tDCS	Transcranial direct current stimulation
atDCS	Anodal transcranial direct current stimulation
ctDCS	Cathodal transcranial direct current stimulation
OxS	Oxidative Stress
ROS	Reactive Oxygen Species
FIPE	Federazione Italiana Pesistica, Italian Weightlifting Federation
IL-6-U	Interleukin 6 in Urine
8-iso-PGF2α	8-isoprostane concentration
HPLC	high-pressure liquid chromatography
Borg-RPE	BORG Rate of Perceived Exertion scale
VAS	Visual Analogue Scale

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Authors' contributions

R.dD. contributed to Conceptualization, Methodology, Validation, Investigation, Writing - Original Draft. M.P. contributed to Conceptualization, Methodology, Software, Data Curation, Visualization, Writing - Original Draft. M.G. contributed to Data Curation, Formal analysis, Writing - Original Draft, Writing - Review & Editing. C.T. contributed to Data Curation, Formal analysis, Writing - Original Draft, Writing - Review & Editing. R.F. contributed to Methodology, Data Curation. A.V. contributed to Methodology, Formal analysis. C. D. contributed to Methodology, Formal analysis. S. P. contributed to Formal analysis, Visualization. A.B. contributed to Validation, Investigation. A.P. contributed to Validation, Supervision, Writing - Review & Editing. S.M. contributed to Conceptualization, Software, Data Curation, Writing - Original Draft, Writing - Review & Editing. S.M.S. contributed to Conceptualization, Data Curation, Visualization, Writing - Original Draft, Supervision. All authors, except A.B. (deceased) read and approved the submitted version of the manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the institutional review board of the Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico di Milano (approval number J274-2022). Written informed consent was obtained from all participants prior to study enrolment.

Consent for publication

All participants provided written informed consent for the publication of potentially identifying images and/or personal or clinical information in this article.

Competing interests
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Author details
[1]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[2]Institute Research, Innovation and Enterprises, Area Science Park, Trieste, Italy
[3]Dipartimento di Ingegneria e Architettura, Università degli studi di Trieste, Trieste, Italy
[4]"Aldo Ravelli" Center for Neurotechnology and Experimental Brain Therapeutics, Department of Health Sciences, University of Milan, Via Antonio di Rudinì 8, Milan 20142, MI, Italy
[5]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan 20122, Italy
[6]ASST Santi Paolo e Carlo, University Hospital, Milan 20142, Italy
[7]Department of Oncology and Emato-Oncology, University of Milan, Milan 20122, Italy
[8]Institute of Clinical Physiology, National Research Council (CNR), Milan, Italy
[9]Associazione Sportiva Dilettantistica Alex Club, Federazione Italiana Pesistica (FIPE), Via Privata Mottarone, 2, Milano 20155, Italy

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