EFFECTS OF COMBINED PLYOMETRIC AND SPEED TRAINING ON CHANGE OF DIRECTION, LINEAR SPEED, AND REPEATED SPRINT ABILITY IN YOUNG SOCCER PLAYERS: A PILOT STUDY

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Abstract:

It has been well established that plyometric and speed training have positive impacts on fitness parameters in soccer players. The aim of this study was to compare short-term effects of a combined plyometric and speed training implemented on the same or separate days of a week on change of direction (COD), linear speed (LS), and repeated sprint ability (RSA) in young soccer players. Twenty-four male players from the same U19 soccer team were distributed into one control group (CG; n=7, soccer training only) and two experimental groups performing plyometric and speed exercises on the same (CDG; n=8) or separate days (CWG; n=9) during a 6-week preparation period. Very likely moderate within-group COD improvements were observed in the CDG (ES -0.94 [-1.47 to -0.41]) and CWG (ES -0.97 [-1.52 to -0.42]) groups. Possibly small within-group RSA improvements were also observed in the CWG (ES -0.24 [-0.64 to 0.16]) and CDG (ES -0.31 [-0.79 to 0.17]) groups. CWG and CDG groups showed possibly small (ES -0.28 [-0.62 to 0.06]) and very likely moderate (ES -0.80 [-1.28 to -0.32]) within-group LS improvements following the intervention, respectively. In between group analysis, a likely moderate (ES 0.71 [0.03 to 1.39]) greater LS improvement was observed in the CDG group than in the CWG group. It is suggested to supplement normal soccer training with combined plyometric and speed exercises to improve COD, LS, and RSA performance and to implement these exercises in the same session to improve LS with a greater effect.

Key words: association football, performance, agility, concurrent training, team sports, youth soccer

Introduction

Soccer is a high-intensity intermittent sport that requires both physical and technical capabilities during match play (Stolen, Chamari, Castagna, & Wisloff, 2005). The intermittent nature of the sport places high demands on the aerobic pathways for most of game time (Reilly, Bangsbo, & Franks, 2000). However, soccer players are also required to perform short duration high-intensity activities such as accelerations, decelerations, and change-of-direction (COD) that rely heavily on anaerobic pathways (Rampinini, Coutts, Castagna, Sassi, & Impellizzeri, 2007b). These high-intensity activities usually occur every 4-6 seconds interspersed with short recovery periods during a match (Mohr, Krustrup, & Bangsbo, 2005). Maximal linear sprints typically occur every 90 s, each lasting from 2 to 4 s (Stolen, et al., 2005). The capacity of players for performing these high-intensity and short-duration activities influences soccer match physical performance (Reilly, et al., 2000; Strøyer, Hansen, & Klausen, 2004). Faude, Koch, and Meyer (2012) reported that at ~ 83% of cases, a straight sprinting is the most frequent action preceding a goal. The
capacity of soccer players to sprint repeatedly with short duration of recovery between sprints is termed repeated sprint ability (RSA) (Girard, Mendez-Villanueva, & Bishop, 2011) and has been deemed to be an important performance variable in soccer (Rampinini, et al., 2007a). This is evident in an inverse large association observed between RSA mean time and very high-intensity running performance (r = -0.60) in professional soccer players (Rampinini, et al., 2007a). Furthermore, it has been shown that professional soccer players have better RSA performance (indicated by mean sprint time, best sprint, and % sprint decrement) than their amateur counterparts (Impellizzeri, et al., 2008).

Despite the relevance of COD, RSA, and linear speed (LS) to soccer performance, regular soccer training alone does not appear to cause improvements in these variables (Hammani, Negra, Aouadi, Shephard, & Chelly, 2016; Hermassi, et al., 2014; Marques, Pereira, Reis, & van den Tillaar, 2013; Ramirez-Campillo, et al., 2015). Therefore, it appears that specificity of sports training, such as protocols targeting COD, RSA, LS, is warranted to improve those abilities (Asadi, Arazi, Young, & De Villarreal, 2016; Peterson, Alvar, & Rhea, 2006). Specific plyometric and speed training protocols have been utilized to supplement regular soccer training to enhance powerful actions such as sprinting and jumping associated with soccer performance (Beato, Bianchi, Coratella, Merlini, & Drust, 2018; Hammani, et al., 2016; Marques, et al., 2013). Furthermore, specific plyometric and speed exercises have been shown to improve short duration explosive actions such as acceleration, LS, and jumping (Asadi, et al., 2016; Beato, et al., 2018). However, RSA is a complex fitness variable that is not only dictated by the energy systems but also by neuromuscular factors such as rate of force development (Girard, et al., 2011). Thus, supplementing soccer training with plyometric and speed exercises has been shown to improve RSA in team sport athletes (Buchheit, Mendez-Villanueva, Delhomel, Brughelli, & Ahmadi, 2010a; Hermassi, et al., 2014; Rey, Padrón-Cabo, & Fernández-Penedo, 2017). Indeed, specific speed or plyometric exercise protocols when used separately may cause improvements in isolated performance variables such as RSA or jumping (Buchheit, Mendez-Villanueva, Delhomel, et al., 2010a). Therefore, researchers have implemented these exercises in a combined approach to improve these variables simultaneously (Beato, et al., 2018; Marques, et al., 2013; Monsef Cherif, Chaatani, Nejloua, Gomri, & Abdallah, 2012). Monsef Cherif et al. (2012) showed that combined plyometric and speed training improved jumping ability, sprint performance, and RSA in professional handball players. Similarly, Beato et al. (2018) also showed that combined speed and plyometric exercises improved sprinting performance with larger effects (range: -0.51 to -0.29 vs. -0.22 to -0.15, for 10 m, 20 m, and 40 m intervals) than isolated speed protocol in elite youth soccer players. Furthermore, Marques et al. (2013) examined the effect of a six-week combined speed and plyometric program in young soccer players and found that training-induced improvements in running speed could also be transferred to soccer.

Research has shown that sprint performance is enhanced after a preload stimulus (e.g., plyometric exercises) due to the “postactivation potentiation” (PAP) phenomenon (Bevan, et al., 2010). This phenomenon is defined as an acute enhancement of muscle function after implementing a preload stimulus (Hodgson, Docherty, & Robbins, 2005). Therefore, implementing sprinting exercises after plyometric exercises within a training session in the combined approach may enhance anaerobic performance variables such as COD, LS, and RSA to a greater extent. However, to the best of our knowledge, no study has yet examined the effects of the combined plyometric and speed training on either the same day or separate days of a training cycle on anaerobic performance. Given the relevance of such analysis, the aim of this study was to compare the effects of the combined plyometric and speed training implemented on either the same or separate days in a week on change of direction, linear speed, and repeated sprint ability in young soccer players.

**Methods**

In this pre-post parallel groups design, the soccer team underwent three different interventions during a 6-week pre-season phase. The training load (training plan) was programmed by one of the authors, being a certified strength and conditioning specialist (CSCS), after reviewing related research and studying the training background of players to accomplish similarity with their previous works and also after considering real training programs recently performed by the team in order to achieve higher external validity. Before the intervention, players performed a maximal high-intensity intermittent endurance running capacity test and were distributed in three homogenous groups accordingly. Physical tests including COD, LS, and RSA were conducted before and after the intervention phase to examine training-induced changes in the dependent variables. One familiarization session was performed before the first testing session to habituate the players with all the fitness tests. All testing sessions were conducted on an indoor track at the same time (i.e., ~11-12 a.m.) with similar environmental conditions (temperature 18-20°C, relative humidity 10-15%). A standardized warm-up activity including 8 min of easy jogging, 5 min of lower limb dynamic stretching, and 5 min of progressive acceleration and sprinting trials preceded the tests. Pre-tests were executed during two sessions.
as 1) anthropometric and high-intensity intermittent running capacity tests, and 2) anaerobic tests (i.e., LS, COD, and RSA). The pre-test sessions were interspersed with 72 hours of rest and conducted before the experiment. Post-test anaerobic session was conducted four days after the last training session with the same protocol implemented in the pre-test. In all tests, the players were instructed to be well hydrated, to avoid eating a large meal or consuming caffeine three hours prior to testing.

**Participants**

Twenty-four soccer players participated in the present study. All players were members of the same soccer team competing in the second division of the Iran league in U19 age category. Players had regular 3-6 on-field training sessions a week for the last year prior to data collection. The players were distributed into three groups: a control group (CG) participated in a usual soccer training program and two experimental groups performed the combined plyometric and speed training on either a weekly (CWG) or daily (CDG) basis. Players’ characteristics are shown in Table 1. All players were informed of the experimental risks, and all signed an informed consent document before the investigation. The protocol was approved by the local research ethics committee, and the study conformed with the Declaration of Helsinki.

**Data collection**

**Training**

High-intensity intermittent endurance running capacity, COD, LS, and RSA were tested in this experiment via 30-15 Intermittent Fitness Test (30-15IFT, VIFT) (Buchheit, 2008), 505 COD (Stewart, Turner, & Miller, 2014), 30-meter linear sprint (Rey, et al., 2017), and 6 reps of 30-meter linear sprints interspersed with 25 s of active recovery (Girard, et al., 2011), respectively. The subjects were instructed not to participate in any official matches or high intensity activities 72 hours before the assessments. All groups of players had five weekly training sessions during the experiment. The CDG and CWG groups performed plyometric and speed training sessions in either the same or separate weekly training sessions, whereas CG did not perform any type of plyometric or speed exercises during the experiment. Weekly training plan during the intervention is illustrated in Table 2. All training sessions were preceded with a standardized warm-up including general activities as well as specific exercises adjusted to the main aim of the given session. The small-sided game (SSG) exercise included 3 sets of 3 min with the 4 vs. 4+goalkeeper (GK) formats interspersed with 3 min of passive recovery phases. The games were played within a 90 m² area on the natural turf surface. No coach encouragement or task constraints were applied to SSG sessions. The number of series for plyometric and speed exercises was increased bi-weekly and the progression is shown in Table 3. The volume of all training modalities including physical and tactical parts were kept similar for all players.

**Testing**

30-15 Intermittent Fitness Test (30-15 IFT)

The 30-15IFT was used to obtain baseline maximal high-intensity intermittent endurance running capacity of the players prior the experiment. 30-15IFT has been deemed to be a valid maximal test in team sports athletes (Buchheit, 2008). 30-15IFT has been shown to be sensitive to different physiological and locomotor profile variables including aerobic power, acceleration, deceleration, jumping, change of direction and recovery abilities (Buchheit, 2010). Therefore, 30-15IFT was used as a multifactorial reference test to divide players in three homogenous groups. All stages of this test consist of 30 s running with 15 s active recovery. The first stage started with 8 km·h⁻¹ speed, and velocity was progressively increased by 0.5 km·h⁻¹ in each stage. Players were instructed to adjust their

| Variable | CG         | CDG         | CWG         |
|----------|------------|-------------|-------------|
| Number   | 7          | 8           | 9           |
| Age (years) | 17.6 (0.4) | 17.8 (0.8)  | 17.8 (0.6)  |
| Body mass (kg) | 66.2 (7.8)  | 63.1 (5.4)  | 64.2 (6.6)  |
| Body height (cm) | 181.1 (6.1)  | 177.1 (5.8)  | 173.8 (4.5)  |
| BMI (kg·m⁻²) | 20.1 (1.7)  | 20.4 (2.0)  | 20.9 (2.4)  |
| VIFT (km·h⁻¹) | 17.7 (0.4)  | 17.8 (1.1)  | 17.8 (1.2)  |

Note. VIFT is the maximal velocity during the last stage of 30-15 Intermittent Fitness Test. BMI is body mass index. CG: control group, CWG: combined weekly group, CDG: combined daily group.

| Group | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday | Sunday |
|-------|--------|---------|-----------|----------|--------|----------|--------|
| CG    | TE/TA  | TE/TA   | Day off   | TE/TA    | Day off| TE/TA    | SSG & TE/TA |
| CWG   | TE/TA  | Plyo & TE/TA | Day off     | TE/TA    | Day off| Speed & TE/TA | SSG & TE/TA |
| CDG   | TE/TA  | TE/TA   | Day off   | TE/TA    | Day off| Plyo & Speed | SSG & TE/TA |

Note. TE/TA: technical and tactical training; Plyo: plyometric training; SSG: small-sided game. CG: control group, CWG: combined weekly group, CDG: combined daily group.
running speed to an auditory signal. In this test, the subjects continue running until exhaustion, which is noted by the inability to continue with the imposed running speed. The maximal speed reached during the last completed stage was recorded as the final performance.

505 COD Test

The 505 test was utilized to measure COD and was conducted per established methods (Draper & Lancaster, 1985). Players were instructed to accelerate 10 m from a standing position through the timing gate placed at the 5-m mark. After passing the 5-m marker, the players planted and turned 180° with their preferred foot to run back passing the timing gate again. The time for a shuttle 5-meter was recorded as the players’ COD ability. The players were instructed to perform this test as quickly as possible for three trials. A 5-min recovery was given between each trial. The best performance of the three trials was recorded as the final score.

Repeated Sprint Ability Test

Repeated sprint ability was measured using six repetitions of 30-meter linear sprints interspersed with 25 s of active recovery. Players were instructed to sprint with their maximal effort and after each sprint instructed to jog slowly back to the starting position. Players were given a notice 5 s before the next sprint to be ready. Timing gates were positioned 30 meters apart and players were instructed to start from 0.5-meter line before the starting line. The sum of sprints’ times in seconds was collected as a general measure of RSA as recommended (Girard, et al., 2011). The best sprint performance (i.e., first run) of RSA was recorded as the player’ LS.

Statistical analyses

The results are presented in text, tables and figures as Mean ± SD or 90% confidence intervals (CI) where specified. Within-group changes and between-group differences in changes of COD, LS, and RSA were expressed as percentage changes and standardized differences as Cohen’s d (effect size, ES, 90% CI) (Cohen, 1988). Magnitude-based inference approach was used for interpreting all changes and/or differences (Batterham & Hopkins, 2006). For all between-group analyses, pre-test results were controlled in the analysis as covariates. Threshold values for ES were < 0.2: trivial; 0.2-0.6: small; 0.6-1.2: moderate; >1.2: large (Batterham & Hopkins, 2006). Probabilities were calculated to indicate whether the true change was lower than, similar to, or higher than the smallest worthwhile change (SWC) (Hopkins, Marshall, Batterham, & Hanin, 2009). The scale of probabilities was as follows: 25-75%: possible; 75-95%: likely; 95-99%: very likely; >99%: almost certain (Hopkins, et al., 2009). The probabilities were used to make a qualitative probabilistic mechanistic inference about the true effect: if the probabilities of the effect being substantially positive and negative were both >5%, the effect was reported as unclear; the effect was otherwise clear and reported as the magnitude of the observed value.

Results

Pre- and post-values of dependent variables are presented in Table 4. Trivial within-group changes were observed in CG for COD (-0.2%, 90% confidence interval [-1.4 to 1.0]), effect size, ES, -0.04 [-0.27 to 0.19]), LS (1.2%, [-1.0 to 3.4]), ES 0.18 [-0.15 to 0.51]), and RSA (0.2%, [-1.2 to 1.6]), ES 0.04 [-0.24 to 0.32]) (Figure 1). Very likely moderate within-group COD improvements were observed in CDG (-4.2%, [-6.4 to -1.8]), ES -0.94 [-1.47 to -0.41]) and CWG (-5.0%, [-7.7 to -2.2]), ES -0.97 [-1.52 to -0.42]) groups. CWG and CDG groups showed possibly small (-1.5%, [-3.3 to 0.3%]), ES -0.28 [-0.62 to 0.06]) and very likely moderate (-4.9%, [-7.7 to -2.0%]), ES -0.80 [-1.28 to -0.32]) within-group LS improvements following the intervention, respectively (Figure 1). Possibly small within-group RSA improvements were also observed in CWG (-1.2%, [-3.3 to 0.8]), ES -0.24[-0.64 to 0.16]) and

Table 3. Plyometric and speed training plan of the 6-week phase

| Weeks | Double-leg LJ | One leg LJ | Double-leg VJ | Lateral BH | Speed exercises |
|-------|--------------|------------|--------------|------------|----------------|
| 1-to-2 | 3×3 reps/45s | 2×3 reps/45s | 3×4 reps/45s | 3×2 reps/45s | 10 m LS reps/30s r |
| 3-to-4 | 4×3 reps/45s | 4×3 reps/45s | 4×2 reps/45s | 4×3 reps/45s | 10 m LS reps/45s r |
| 5-to-6 | 5×3 reps/45s | 6×3 reps/45s | 5×4 reps/45s | 5×2 reps/45s | 10 m LS reps/30s r |

Note. LJ: long jump, VJ: vertical jump, BH: barrier hop, LS: linear sprint, COD: change of direction, r: rest period. The first numeral denotes the number of series and the second one the number of repetitions (reps), e.g., 3×3 is 3 series of 3 repetitions. 2-to-3 min recovery was implemented between all the series.
CDG (-1.4%, [-3.6 to 0.8%]), ES -0.31 [-0.79 to 0.17]) and CWG (5.0%, [1.9 to 8.3%]), ES 0.85 [0.32 to 1.37]) than in CG (Figure 2/A, C). A likely moderate (3.5%, [0.1 to 7.1%]) greater LS improvement was also observed in CDG group over CWG group (Figure 2/B).

**Discussion and conclusions**

The purpose of this study was to compare the short-term effects of the combined plyometric and speed exercises implemented on the same or separate weekly days on COD, LS, and RSA in young soccer players. Our results suggested that supplementing soccer training with the combined plyometric and speed exercises enhanced RSA, LS, and COD with small-to-moderate effects. This study also showed that combining plyometric and speed training in one session is moderately more effective than implementing them on separate weekly days when aiming to improve LS.

In the present study, both the CDG and CWG groups showed very likely moderate enhancements in COD (Figure 1). These COD improvements observed in the CDG and CWG groups were very likely greater than in the CG group with moderate...
effects with moderate reductions in COD time (ES, ~ 0.7) found by Yanci, Castillo, Iturricastillo, Ayarra, and Nakamura (2017), and Ramirez-Campillo et al. (2015) when implemented 1-day-per-week plyometric and 2-day-per-week combined vertical and horizontal exercises, respectively. Our results are however in contrast to findings of Beato et al. (2018) who reported only trivial changes in COD after the 6-week combined plyometric and directional training intervention. Although the training protocol, the intervention period, and subjects’ characteristics of the latter study were very similar to our study, their results, in terms of changes in 505 COD test (i.e., ~ 4.7s), were surprisingly greater than the values observed here and in the literature (~ < 3s) (Stewart, et al., 2014; Thomas, French, & Hayes, 2009). Therefore, it is difficult to compare and make a valid conclusion considering the results reported by Beato et al. (2018). While Ramirez-Campillo et al. (2015) showed a moderate change in COD after a 2-day-per-week intervention, our results are more consistent with the findings of Yanci et al. (2017) who showed that only one training session a week is enough to enhance COD, LS, and RSA. No substantial differences were observed between the weekly and daily application of the combined plyometric and speed training on changes in COD. These results suggest that only one-weekly plyometric and speed training, if designed appropriately, is enough to enhance COD with moderate effects (Asadi, et al., 2016). The mechanism responsible for improvements in COD in our study may be associated with neural adaptations and enhancement of motor-unit recruitments (Aagaard, Simonsen, Andersen, Magnusson, & Dyhre-Poulsen, 2002). Furthermore, improvements in COD may also be attributed to mechanical factors such as improvements in the rate of force development (Miller, Herniman, Ricard, Cheatham, & Michael, 2006; Sheppard & Young, 2006) and in movement efficiency (Young, McLean, & Ardagna, 1995), caused by stretch-shortening cycle exercises such as plyometric and COD drills implemented in our study.

Trivial changes in LS was observed in CG group. CWG and CDG groups experienced possibly small and very likely moderate improvements in LS, respectively. CDG group showed a likely moderately greater enhancement in LS than CWG group. Unchanged LS observed here in CG group is consistent with previous studies (Marques, et al., 2013; Ramirez-Campillo, et al., 2015) in which soccer training did not cause significant changes in sprint performance. To improve sprint performance, specific sprint training should adhere to the principle of specificity and progression in overload; therefore, normal soccer training can just maintain performance but it is not sufficient to improve linear speed in soccer players (Rumpf, Lockie, Cronin, & Jalilvand, 2016). The small to moderate improvements in LS observed in this study are in line with similar results found by Beato et al. (2018) (ES: -0.29) and Ramirez-Campillo et al. (2015) (range ES: -0.30; -0.63). These results are also similar to Yanci et al. (2017) who reported moderate improvements in sprinting speed (ES: 0.6 to 1.0). Although the sprinting speed in Yanci et al. (2017) was evaluated over a shorter distance compared to our study (15 m vs. 30 m), these observations highlight the value of supplementing normal soccer training with plyometric and speed training to improve leg power (Chelly & Denis, 2001). The moderately greater LS enhancement observed here in the CDG group than in the CWG group also suggest that greater LS improvement may occur if combining plyometric and speed training on a daily versus weekly basis. To our knowledge, the only study that compared the combined plyometric and speed training to isolated speed training was the study of Beato et al. (2018) in which substantial LS enhancement was observed in the combined approach. The reason for training-induced changes in LS when combining plyometric and speed training in one session compared to that in separate weekly-sessions might be pertinent to the “post-activation potentiation (PAP) phenomenon”. Research has shown that sprinting performance is enhanced after a preload stimulus providing adequate recovery is given between the activities due to PAP (Bevan, et al., 2010; Crewther, et al., 2011; Turner, Bellhouse, Kilduff, & Russell, 2015). Although electromyography recording was not measured in this study and the mechanism responsible for these results is again speculative, we may presume that the preload stimulus via plyometric exercises might have enhanced motor-unit excitability or enhanced phosphorylation of the myosin light chains (Gossen & Sale, 2000). Therefore, those players in the CDG group who performed speed exercises after the plyometric exercises within one training session likely performed speed exercises with greater performance favored by PAP and subsequently experienced larger enhancements in LS. However, it needs to be mentioned that players in CWG might have also experienced PAP after first repetitions of sprinting in their training protocol, but CDG have logically received relatively stronger PAP thanks to plyometric exercises performed before their sprinting repetitions. Although the same trend might had been expected for COD, our results were likely due to the possible fatigue-induced impairment in PAP (Bevan, et al., 2010) since COD exercises were implemented in the final stages of combined exercises (Table 3).

Our results showed that usual soccer training does not cause any substantial enhancement in RSA. However, supplementing RSA with the combined plyometric and speed training, whether implementing it on the same or on separate days of a
weekly training cycle, possibly enhanced RSA with small effect during the 6-week preparation phase. No changes in RSA were observed in this study for usual training, which was similar to the findings of Hammami et al. (2016) in soccer players and also Hermassi et al. (2014) in elite handball players. Our results, however, are not consistent with the study by Yanci et al. (2017) in which large improvement was observed for RSA total time (ES: 1.5) due to normal training in futsal players. It seems that normal futsal training, which usually comprises SSGs in 5 vs. 5 regimens (Barbero-Alvarez, Soto, Barbero-Alvarez, & Granda-Vera, 2008), is responsible for this large improvement in RSA. It has been reported that SSG training can enhance RSA in team sport athletes due to its high demand on the metabolic systems (Owen, Wong, Darren, & Dellal, 2012; Seitz, Rivière, De Villarreal, & Hafl, 2014). The small improvement in RSA observed in our study when supplementing normal soccer training with the combined plyometric and soccer training is in agreement with significant changes observed in the study by Monsef Cherif et al. (2012) after implementing the combined approach. This is not surprising since RSA has been previously shown to be improved by supplementing normal training with both the plyometric (Buchheit, Mendez-Villanueva, Delhomel, et al., 2010a; Hermassi, et al., 2014) and speed (Buchheit, Mendez-Villanueva, Quod, Quesnel, & Ahmaidi, 2010b; Rey, et al., 2017) exercises. Although changes in jump performance were not measured as a way to track force production adaptation in this study, the moderate COD improvement as well as small-to-moderate LS improvements in the CWG and CDG groups may suggest that RSA improvement has been obtained both from explosive force and sprinting mechanisms (Girard, et al., 2011) targeted during plyometric (Asadi, et al., 2016) and speed (Buchheit, Mendez-Villanueva, Quod, et al., 2010b) training, respectively.

This study showed that normal soccer training does not cause any substantial improvement in COD, LS and RSA, but supplementing it with combined plyometric and speed exercises can enhance these performance variables with small to moderate effects. Our results also suggest that combining plyometric and speed training in the same weekly session is more effective than implementing them on separate weekly days when the aim is to improve LS. Therefore, strength and conditioning professionals working with young soccer players are encouraged to supplement normal training with the combined plyometric and speed exercises. It is also recommended to implement these exercises in the same weekly session to improve linear speed with greater effects.

**Conflict of interest**

The authors declare no conflict of interest.

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