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RESEARCH ARTICLE

Fluoxetine impairs muscular strength, power and endurance performance particularly when it is co-ingested with caffeine: a case study

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Fluoxetine;
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Resistance Training;
Sport performance;
Case Report.

Fluoxetine impairs muscular strength, power and endurance performance particularly when it is co-ingested with caffeine: a case study

ABSTRACT

Introduction: Fluoxetine is a recurrent pharmacotherapy for depression used in athletes since it does not seem to impair sports performance. Some athletes combine this drug with caffeine, however, the combined effect of both drugs remains to be elucidated. This study aimed to explore the combined effect of fluoxetine and caffeine on muscular strength, power, and endurance performance.

Methodology: In this case study, a resistance-trained female was recruited to complete four randomized experimental conditions: a) placebo (PLA); b) placebo and fluoxetine (PLA+FLU); c) caffeine (CAF); d) caffeine and fluoxetine (CAF+FLU). The participant was provided with 20 mg/day of fluoxetine and 3 mg/kg of body mass of caffeine or maltodextrin (placebo) 60 minutes after performing the tests. The participant performed for bench press and back squat exercises a muscular strength and power test at 25%, 50%, 75% and 90%1-repetition-maximum (1RM), followed by a muscular endurance assessment at 65% and 85%1RM.

Results: CAF+FLU reduced mean velocity and power output in both exercises at 75% and 90%1RM in muscular strength and power tests and at 85%1RM in the muscular endurance test. While PLA+FLU and CAF+FLU administration reduced peak velocity and mean and peak power output at 25%1RM in the muscular strength and power test and at 65%1RM in the muscular endurance test.

Conclusions: Fluoxetine may counteract the ergogenic effect of caffeine impairing muscular strength, power and endurance performance. Therefore, although further studies are needed, athletes diagnosed with depression on fluoxetine treatment should reconsider caffeine consumption as a nutritional supplement to enhance performance.

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La fluoxetina reduce la fuerza, potencia y resistencia muscular, especialmente cuando se ingiere junto con cafeína: un estudio de caso

PALABRAS CLAVE

Depresión;

Fluoxetina;

Cafeína;

Entrenamiento de fuerza;

Rendimiento Deportivo;

Estudio de Caso.

RESUMEN

Introducción: La fluoxetina es un fármaco utilizado para la depresión especialmente en deportistas ya que parece no alterar el rendimiento deportivo. Algunos atletas combinan este fármaco con cafeína, sin embargo, el efecto combinado de ambas drogas se desconoce. Este estudio tuvo por objetivo explorar el efecto combinado de fluoxetina y cafeína sobre el rendimiento de fuerza, potencia y resistencia muscular.

Metodología: En este estudio de caso, una mujer entrenada en fuerza realizó cuatro condiciones experimentales: a) placebo (PLA); b) placebo y fluoxetina (PLA+FLU); c) cafeina (CAF); d) cafeína y fluoxetina (CAF+FLU). La participante ingirió 20 mg/día de fluoxetina y 3 g/kg de masa corporal de cafeína o placebo (maltodextrina), 60 minutos antes de realizar los test. La participante realizó un test de fuerza y potencia muscular al 25%, 50%, 75% y 90% de 1-repetición-máxima (1RM), seguido de un test de resistencia muscular al 65% y 85% de 1RM, en ambos casos para los ejercicios de *press* de banca y sentadilla.

Resultados: CAF+FLU redujo la velocidad y potencia media en *press* de banca y sentadilla al 75% y 90% de 1RM en el test de fuerza y potencia muscular, y al 85% en el test de resistencia muscular. Mientras que la administración de PLA+FLU y CAF+FLU redujo el pico de velocidad y potencia al 25% de 1RM en fuerza y potencia muscular y al 65% de 1RM en resistencia muscular.

Conclusiones: La fluoxetina contrarresta el efecto ergogénico de la cafeína sobre la fuerza, potencia y resistencia muscular. Por tanto, aunque más estudios son necesarios, los atletas diagnosticados con depresión bajo tratamiento de fluoxetina deberían reconsiderar el uso de cafeína como suplemento nutricional para mejorar el rendimiento.

KEY MESSAGES

1. Fluoxetine is a commonly used drug to treat depression in athletes since it does not seem to alter sports performance.
2. During competition, some athletes are under fluoxetine treatment, combining this drug with caffeine intake to enhance their performance.
3. Fluoxetine intake reduced muscular strength, power and endurance performance.
4. Fluoxetine intake counteracted the ergogenic effect of caffeine on muscular strength, power, and endurance performance.
5. Athletes diagnosed with depression under fluoxetine treatment should reconsider the use of caffeine as a performance-enhancing nutritional supplement.

CITATION

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INTRODUCTION

It is estimated that there are around 350 million people worldwide suffering from depressive disorders[1]. Elite and even recreational athletes are also exposed to suffer this disease; in fact, the prevalence of depression among athletes is high due to several risk factors such as injuries, career termination, decline in performance, catastrophic performance or even as a consequence of COVID-19 pandemic lockdown[2], observing a more pronounced prevalence in individual sports compared to team sport athletes[3]. Several pharmacotherapies have been developed to treat depression (e.g., Venlafaxine, Imipramine or Fluoxetine). Among them, fluoxetine is a selective serotonin reuptake inhibitor that facilitates neurogenesis in the dentate gyrus of the hippocampus, stimulation required for learning and memory improvement, which counteracts depression[4]. In athletes, fluoxetine is one of the preferred depression treatment drugs since it seems to not improve or impair performance during training or competitions[5].

The case of Simone Biles during the Olympic Games of Tokyo 2020 revealed that some athletes could compete suffering from depression and even being treated with anti-depressant drugs (e.g., fluoxetine). During the course of depression treatment, some athletes draw on nutritional supplementation with ergogenic effects during training or competitions to improve or maintain performance. Caffeine (1,3,7 trimethylxanthine) is one of the most recurred nutritional supplements consumed by athletes of different sports modalities and levels of expertise since this substance improves performance in a myriad of exercise modes[6]. Particularly, caffeine enhances muscular strength, power and endurance performance increasing mean and peak velocities[7].

However, the interaction between anti-depressive drugs (e.g., fluoxetine) and nutritional supplements (e.g., caffeine) has not been explored in the sport performance context. Therefore, this case study aimed to examine the combined effect of fluoxetine and caffeine administration on upper and lower-limb muscular strength, power and endurance performances at different loads. We hypothesized that the ergogenic effect of caffeine would be amplified when it is co-ingested with fluoxetine by retarding caffeine metabolization.

METHODOLOGY

A full description of the experimental design and procedure has been previously published[8].

Participant information

A female participant (aged: 25 yr; body mass: 56.7 kg; fat mass: 13.4 kg) was recruited for this investigation. The participant was diagnosed with depression by a medical doctor who prescribed fluoxetine (Adofen, Ferrer group, Spain) to treat this medical illness. No other medication or drug was prescribed as part of the pharmacotherapy treatment, and the participant did not consume any other substance that may affect neuromuscular performance, the metabolism or bioavailability of caffeine. The inclusion/exclusion criteria can be found elsewhere[8]. The participant reported the following dietary habits: a) Protein/CHO/Fat: 18/61/21 %, b) Caffeine intake: 90 mg/day; and physical activity habits: a) Training experience: 3 years, b) Upper- and lower-body training: 3 days each body part/week, c) Bench press 1RM: 67.5 kg, d) Back squat 1RM: 117,5 kg.

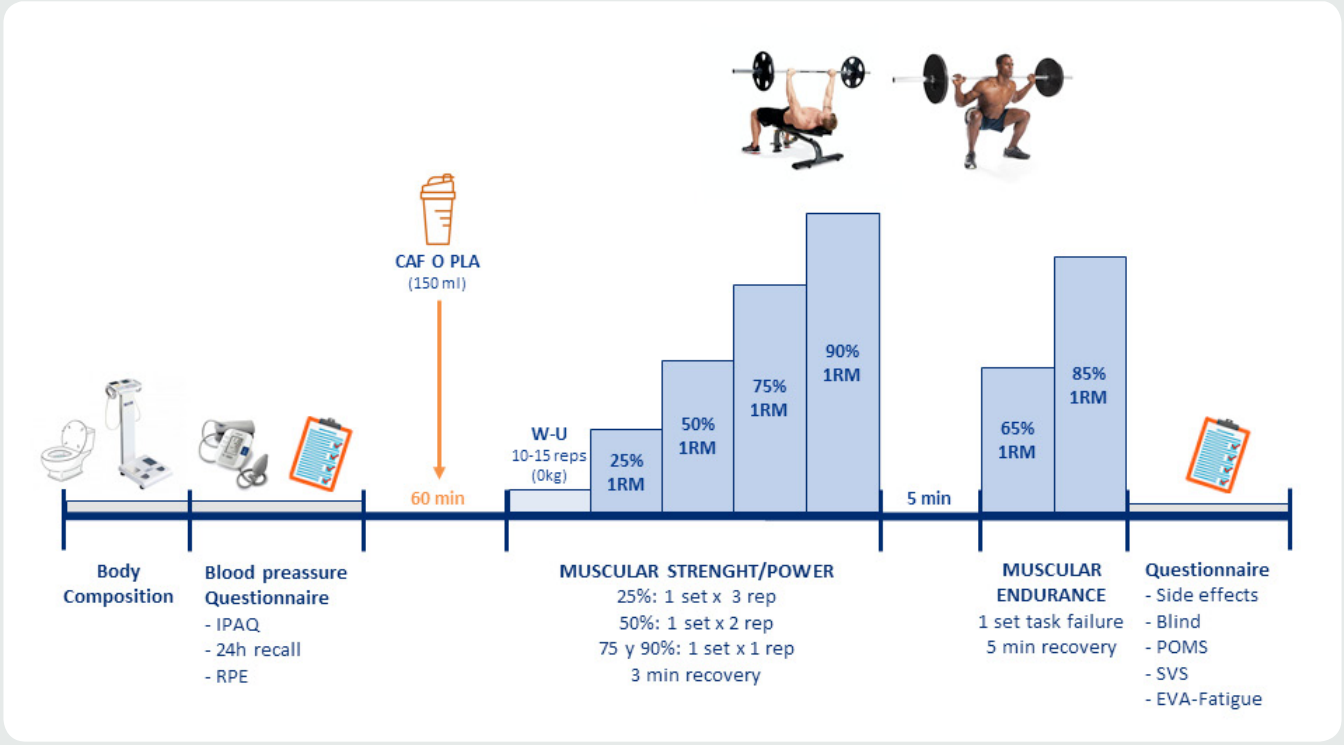
Before study enrolment, all procedures, potential risks or discomfort associated with the experiments were explained to the participant, who then gave their written informed consent. Ethical approval was obtained through the Ethics Committee of Investigation and Animal Experimentation from the University of Alcalá as part of a greater investigation (CEIP/HU/2021/1/006) in accordance with the latest version of the Declaration of Helsinki.

Experimental design and procedure

A cross-over and randomized experimental design was used in this case study. The detailed version of the experimental design and procedure can be found elsewhere[8]. Nonetheless, we describe this section here in brief. The participant reported to the laboratory (044.01.047.0) of the Faculty of Medicine and Health Sciences on five separate occasions. The participant underwent preliminary dietary and physical activity habits and body composition assessments during visit one. Besides, this first visit included a familiarization session where a personal trainer evaluated bench press and back squat exercises and their one-repetition maximum (1RM) for both exercises was obtained.

During visits two to five (Figure 1), the athlete reported to the laboratory at the same time of day (± 30 minutes) and participated in four trials separated by at least 72h to allow a complete recovery and washout period. The participant was assigned to four conditions: a) PLA, 3 mg/kg of body mass of placebo (maltodextrin, HSN, Granada, Spain); b) PLA+FLU, 20 mg/day of fluoxetine (Adofen, Ferrer group, Spain); c) CAF, 3 mg/kg of body mass of caffeine (HSN, Granada, Spain); d) CAF+FLU. The order of the trials was randomized (www.randomized.org). An external researcher was uncharged with elaborating an alphanumeric code assigned to the participant and trial beverages to blind the participant and researchers during the trials.

Figure 1. Experimental procedure.



After 60 minutes of supplements intake, were body composition, physical activity and dietary habits were controlled (Figure 1), the athlete performed muscular strength and power assessment for bench press and back squat exercise at 25%, 50%, 75% and 90% 1-repetition-maximum (1RM), followed by muscular endurance assessment for both exercises at 65% and 85% 1RM using a Smith machine (Multipower, Technogym, Spain) and a linear transductor (Encoder, Chronojump Boscosystem, Italy).

RESULTS

No differences in PLA, PLA+FLU, CAF or CAF+FLU were found for body composition, dietary and physical activity habits. The participant correctly guessed the caffeine ingestion in one of the two trials in which this supplement was ingested. Finally, no mood, adverse or side-effect was reported by the participant, who completed and tolerated the tests without any other related problems.

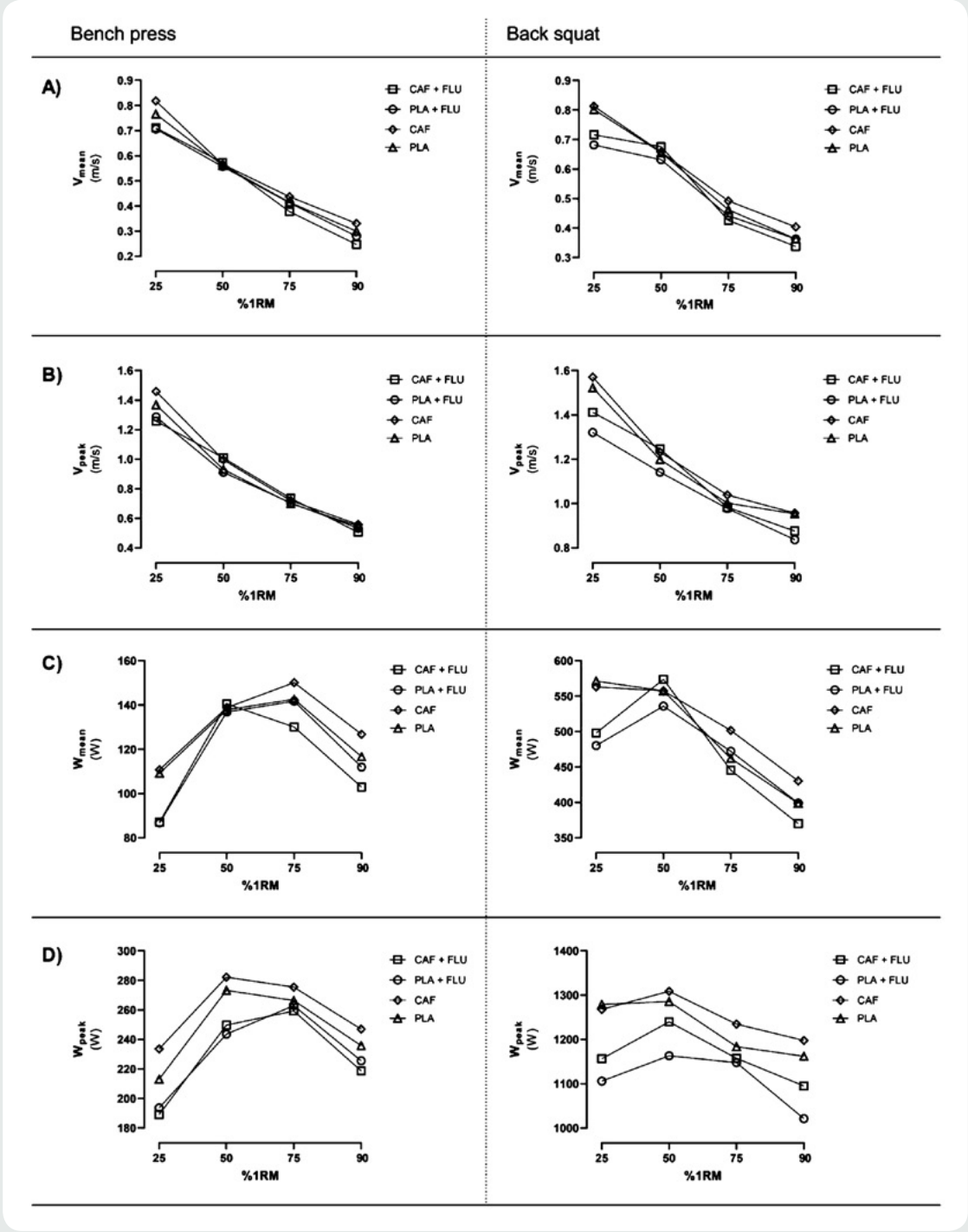
Muscular strength, power and endurance

Figure 2 illustrates differences in muscular strength and power among CAF+FLU, PLA+FLU, CAF and PLA trials. In mean velocity (Vmean), CAF+FLU reduced performance from -13 to -25% compared to CAF and from -5 to -15% compared to PLA+FLU and PLA trials in the bench press and back squat exercises at 75% and 90% 1RM. While FLU administration (CAF+FLU and PLA+FLU) showed a -6 to -16% decrease in mean and peak velocity compared to placebo and caffeine in both exercise types at 25% 1RM.

Similarly, mean power output (Wmean), CAF+FLU reduced performance from -11 to -18% compared to CAF and from -5 to -11% compared to PLA+FLU and PLA trials in both exercises at 75% and 90% 1RM. While, FLU administration (CAF+FLU and PLA+FLU) showed a -8 to -21% decrease in mean and peak power output (Wpeak) compared to placebo and caffeine in both exercise types at 25% 1RM.

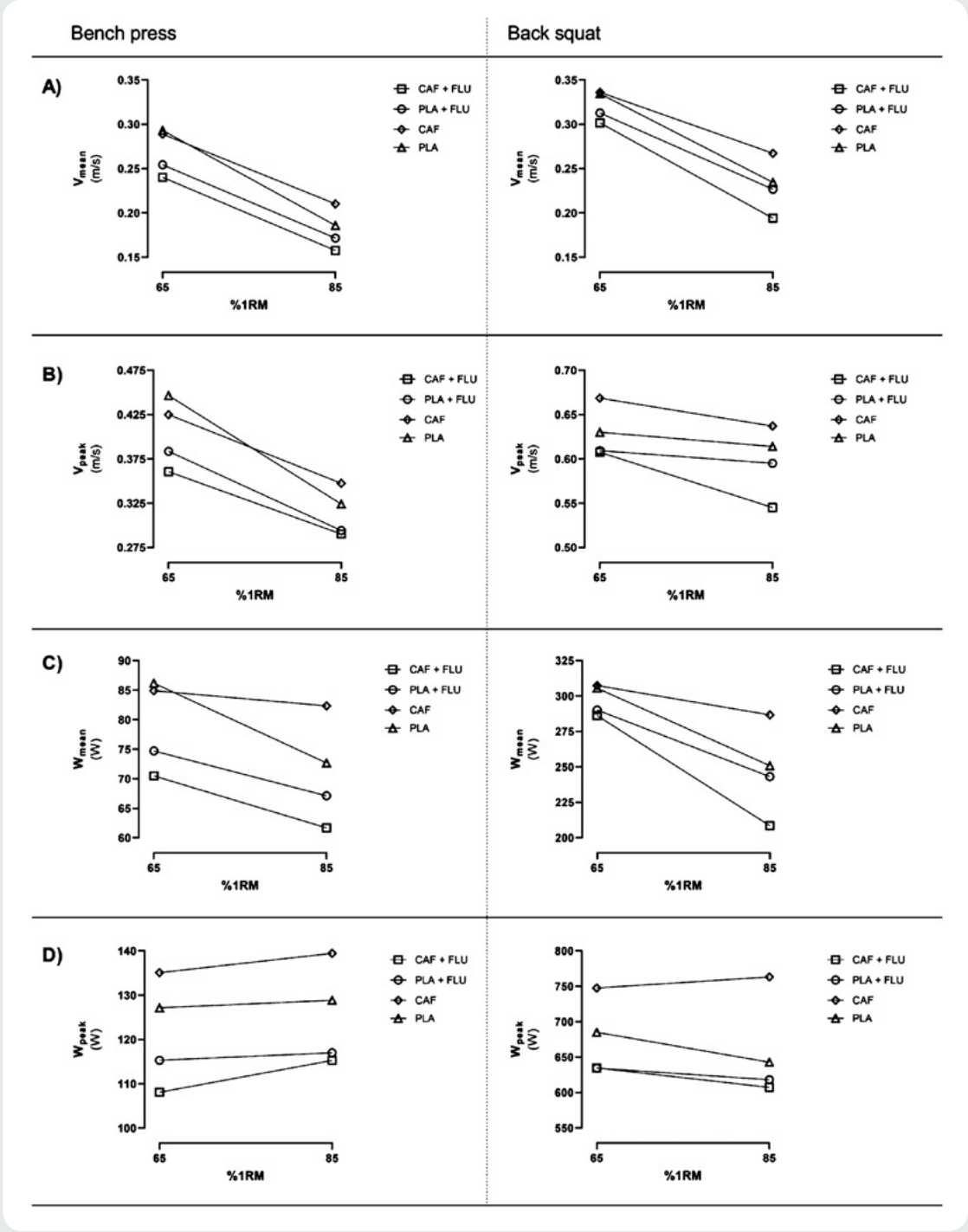
Figure 3 illustrates differences in muscular endurance among CAF+FLU, PLA+FLU, CAF and PLA trials. In Vmean and peak

Figure 2. Differences in muscular strength and power at different loads in bench press and back squat exercises among experimental conditions.



CAF: Caffeine; **CAF+FLU:** Caffeine and fluoxetine; **PLA:** Placebo; **PLA+FLU:** Placebo and fluoxetine; **Vmean:** Mean propulsive velocity; **Vpeak:** Peak propulsive velocity; **Wmean:** Mean power output; **Wpeak:** Peak power output.

Figure 3. Differences in muscular endurance at different loads in bench press and back squat exercises among experimental conditions.



CAF: Caffeine; **CAF+FLU:** Caffeine and fluoxetine; **PLA:** Placebo; **PLA+FLU:** Placebo and fluoxetine; **Vmean:** Mean propulsive velocity; **Vpeak:** Peak propulsive velocity; **Wmean:** Mean power output; **Wpeak:** Peak power output.

propulsive velocity (Vpeak), FLU administration (CAF+FLU and PLA+FLU) showed a -4 to -18% decrease compared to placebo and caffeine in both exercise types at 65% 1RM. While at 85%, CAF+FLU reduced Vmean and Vpeak performance from -17 to -27% compared to CAF and from -7 to -18% compared to PLA+FLU and PLA trials in both exercises.

Similarly, in Wmean and Wpeak, FLU administration (CAF+FLU and PLA+FLU) showed a -7 to -20% compared to placebo and caffeine at 65% 1RM. While, at 85% 1RM, CAF+FLU reduced Wmean and Wpeak performance from -17 to -27% compared to CAF and from -8 to -18% compared to PLA+FLU and PLA trials in both exercises.

DISCUSSION

The purpose of this case study was to evaluate the combined effect of fluoxetine and caffeine administration on upper and lower-limb muscular strength, power and endurance performance at different loads. In muscular strength and power tests, co-ingestion of caffeine and fluoxetine reduced mean velocity and power output at 75% and 90% 1RM performance in both bench press and squat exercises. While FLU administration reduced performance at peak velocity and mean and peak power output at 25% 1RM. Besides, in muscular endurance, fluoxetine administration reduced mean and peak velocity and power output at 65% 1RM, while at 85% 1RM, co-ingestion of caffeine and fluoxetine reduced performance compared to the remaining three trials.

In contrast to what was hypothesized, these results suggest that co-ingestion of caffeine and fluoxetine mitigates the ergogenic effect of caffeine and reduces performance compared to placebo and fluoxetine conditions, particularly at high-load (>75% 1RM). Caffeine is metabolized by the cytochrome P450 (CYP1) family enzymes in the liver[9], whereas fluoxetine inhibits these enzymes[10]. Some studies carried out in animal models support this idea, finding no statistically significant increase in caffeine concentration when fluoxetine + saline was compared to fluoxetine + caffeine intake (404 vs 435 ng/mL) and also an enhanced the antidepressant-like activity of fluoxetine[11]. Altogether, the capacity of fluoxetine to inhibit cytochrome P450 (CYP1) family enzymes[10] and the no statistically significant increase in caffeine concentration after fluoxetine administration found in animal models[11], it may indicate that in humans, fluoxetine ingestion could prolong caffeine bioavailability in blood, and potentially enhancing the ergogenic effect of this nutritional supplement. Nevertheless, the pharmacokinetic interaction of caffeine and fluoxetine seems to cause a toxic effect[12], and in this case study, it was found that the ingestion of caffeine and fluoxetine reduced muscular strength power and endurance performance. Thus, the interaction of both drugs could potentially provoking a central effect that reduces muscular velocity and power output, particularly when the exercise requires the mobilization of high-loads. However, future experimental studies are required to explore this idea.

This investigation presents two major limitations that must be acknowledged. Firstly, the study design. As a case study with a limited sample size (N=1), the results cannot be extrapolated to the entire population of patients under fluoxetine treatment. Secondly, caffeine and fluoxetine presence in blood have not been measured. This information would provide more information about the potential interaction between these substances.

CONCLUSIONS

In this case study, the administration of fluoxetine in a female recreationally-trained participant impaired the ergogenic effect caused by 3 mg/kg of caffeine on muscular strength, power, and endurance performance. Although further experimental studies are needed to explore the interaction between caffeine and fluoxetine, these results may indicate that athletes diagnosed with depression on fluoxetine treatment should be careful when using caffeine as a nutritional supplement to improve performance.

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AUTHORS' CONTRIBUTIONS

A.P.-L. conceived the experiment. C.F., D.V. and A.P.-L. designed the experiment. J.J.M.-A., C.F., D.V. and A.P.-L. collected the data. J.J.M.-A., C.F., S.R.-M., D.V. and A.P.-L. analysed and interpreted the data. J.J.M.-A., S.R.-M. and A.P.-L. drafted the manuscript. All authors read and approved the final version of the manuscript.

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The authors declare that there has been no funding to carry out this study.

COMPETING INTERESTS

The authors state that there are no conflicts of interest in preparing the manuscript.

REFERENCES

(1) Smith K. Mental health: A world of depression. Nature. 2014; 515(7526): 180-1. doi: 10.1038/515180a.
(2) Wolanin A, Gross M, Hong E. Depression in athletes: prevalence and risk factors. Curr Sports Med Rep. 2015; 14(1): 56-60. doi: 10.1249/JSR.0000000000000123.
(3) Pluhar E, McCracken C, Griffith KL, Christino MA, Sugimoto D, Meehan WP. Team Sport Athletes May Be Less Likely To Suffer Anxiety or Depression than Individual Sport Athletes. J Sports Sci Med. 2019; 18(3): 490-6.
(4) Micheli L, Ceccarelli M, D'Andrea G, Tirone F. Depression and adult neurogenesis: Positive effects of the antidepressant fluoxetine and of physical exercise. Brain Res Bull. 2018; 143: 181-93. doi: 10.1016/j.brainresbull.2018.09.002.
(5) Meeusen R, Piacentini MF, Van Den Eynde S, Magnus L, De Meirleir K. Exercise performance is not influenced by a 5-HT reuptake inhibitor. Int J Sports Med. 2001; 22(5): 329-36. doi: 10.1055/s-2001-15648.
(6) Aguilar-Navarro M, Muñoz G, Salinero JJ, Muñoz-Guerra J, Fernández-Álvarez M, Plata MDM, et al. Urine Caffeine Concentration in Doping Control Samples from 2004 to 2015. Nutrients. 2019; 11(2): 286. doi: 10.3390/nu11020286.
(7) Grgic J. Effects of Caffeine on Resistance Exercise: A Review of Recent Research. Sports Med. 2021; 51(11): 2281-98. doi: 10.1007/s40279-021-01521-x.
(8) Ruiz-Fernández I, Valadés D, Dominguez R, Ferragut C, Pérez-López A. Load and muscle group size influence the ergogenic effect of acute caffeine intake in muscular strength, power and endurance. Eur J Nutr. 2023; 62(4): 1783-94. doi: 10.1007/s00394-023-03109-9.
(9) Carrillo JA, Benitez J. Clinically significant pharmacokinetic interactions between dietary caffeine and medications. Clin Pharmacokinet. 2000; 39(2): 127-53. doi: 10.2165/00003088-200039020-00004.
(10) Jeppesen U, Gram LF, Vistisen K, Loft S, Poulsen HE, Brøsen K. Dose-dependent inhibition of CYP1A2, CYP2C19 and CYP2D6 by citalopram, fluoxetine, fluvoxamine and paroxetine. Eur J Clin Pharmacol. 1996; 51(1): 73-8. doi: 10.1007/s002280050163.
(11) Szopa A, Poleszak E, Wyska E, Serefko A, Wośko S, Wlaź A, et al. Caffeine enhances the antidepressant-like activity of common antidepressant drugs in the forced swim test in mice. Naunyn Schmiedebergs Arch Pharmacol. 2016; 389(2): 211-21. doi: 10.1007/s00210-015-1189-z.
(12) Jamal F, Durgam A, Aickareth G, Bajaj R, Mathews M. A Case of Caffeine Intolerance With Long-Term Use of Fluoxetine. Prim Care Companion CNS Disord. 2017; 19(3). doi: 10.4088/PCC.16l02045.