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Creatine monohydrate ingestion-related placebo effects on brief anaerobic exercise performance. A laboratory investigation

Efectos placebo de la ingestión de monohidrato de creatina sobre el rendimiento breve del ejercicio anaeróbico. Una investigación de laboratorio

Efeitos de placebo relacionados com a ingestão de monohidrato de creatina no desempenho de exercício anaeróbico breve. Uma investigação laboratorial

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Resumen: La influencia de los pensamientos de las personas sobre sus acciones, llevó a los investigadores a investigar el efecto placebo sobre el rendimiento en el ejercicio. En el presente estudio se analiza el efecto placebo de la creatina monohidrato sobre el rendimiento en un ejercicio anaeróbico de un minuto de duración en laboratorio mediante el método de doble ciego. Los participantes fueron estudiantes universitarios (n = 79, 64,5% mujeres) que se asignaron aleatoriamente a una de las tres condiciones experimentales: 1) intervención (ingestión de creatina monohidrato disuelta, n = 26); 2) placebo (ingestión de almidón de maíz disuelto, creyendo que es creatina , n = 26); y 3) grupo control sin intervención (ingestión de agua potable solamente, n = 27). Después de establecer la línea base, los participantes tomaron sus respectivas bebidas y 40 minutos más tarde se repitió el ejercicio de 1 minuto de duración. Si bien el análisis de varianza no reveló diferencias entre los grupos entre el rendimiento real y el percibido, este último se vinculó, mediante análisis de correlación, a las expectativas de los participantes en relación con el rendimiento en la segunda prueba realizada. Dos tercios de los participantes consideraron que su rendimiento mejoraría en la prueba de ejercicio real, sin embargo, estas expectativas no estuvieron relacionadas con la ingesta de creatina. Los resultados sugieren que: (1) una dosis única de creatina monohidrato no afecta al rendimiento anaeróbico; (2) en la condición de bajo desafío y baja importancia subjetiva, no emergió el efecto placebo debido, probablemente, a la falta de expectativas evocadas sobre los efectos de la creatina.
Palabras clave: Cardiovascular / Cardiorrespiratorio, Eficiencia, Fatiga, Psicología, Fuerza

Abstract: People's thoughts influence their action that led researchers to investigate the placebo effect in exercise performance. In the current study the placebo effects of creatine monohydrate on a one-minute anaerobic step-exercise performance were examined in a double blind laboratory inquiry. University students (n = 79, 64.5% women) were randomly assigned to one of three experimental conditions: 1) intervention (ingestion of 80 mg/kg dissolved creatine monohydrate, n = 26), 2) placebo (ingestion of dissolved corn starch, thought to be creatine, n = 26), and 3) no-intervention control (ingestion of drinking water only, n = 27). After a baseline measurement, participants have consumed their respective drinks and 40 minutes later the 1-minute exercise was repeated. While analysis of variance revealed no group level differences in actual and perceived change in performance, the latter was linked to participants' expectations regarding performance on the second exercise test in the correlation analysis. Two thirds of the participants in the current study believed that their performance would improve in the actual test-exercise. However, these expectations were not linked to creatine ingestion. These findings suggest that (1) a single dose of creatine monohydrate does not affect anaerobic performance, (2) in low-challenge and low-subjective-importance "artificial" research conditions sufficient expectations could not be evoked, and probably due to the lack of creatine-related expectations the placebo effects did not emerge.
Key words: Cardiovascular/Cardiorespiratory, Efficiency, Fatigue, Psychology, Strength.

Resumo: A influência dos pensamentos das pessoas sobre suas ações, levou os pesquisadores a investigar o placebo efeito sobre o desempenho do exercício. No presente estudo, a creatina mono-hidrato de placebo no desempenho no exercício anaeróbio de um minuto no laboratório pelo método de efeito duplo-cego é analisada. Os participantes eram estudantes universitários (n = 79, 64,5% mulheres) que foram atribuídos aleatoriamente a uma de três condições experimentais atribuída: 1) intervenção (ingestão de creatina monohidratada dissolvida, n = 26); 2) placebo (amido de milho dissolvido ingestão, acreditando que a creatina, n = 26); e 3) grupo de controlo sem intervenção (apenas ingestão de água potável, n = 27). Depois de estabelecer a linha de base, os participantes tomaram suas bebidas e 40 minutos depois do exercício de 1 minuto de duração repetido. Enquanto a análise de variância não revelou diferenças entre os grupos de entre o desempenho real e percebidos, a última foi ligada por análise de correlação, as expectativas dos participantes em relação ao desempenho no segundo teste realizado. Dois terços dos participantes sentiram que seu desempenho iria melhorar no teste de esforço real, no entanto, essas expectativas não foram relacionados com a ingestão de creatina. Os resultados sugerem que: (1) uma única dose de mono-hidrato de creatina não afecta o desempenho anaeróbio; (2) a condição sob desafio e menor importância subjetiva, surgiu o efeito placebo, provavelmente devido à falta de expectativas evocado sobre os efeitos da creatina.
Palavras chave: Cardiovascular / Cardiorespiratória, Eficiência, Fadiga, Psicologia, Força.

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Expectancy and conditioning, which are not independent of one another, are the two major underlying components of placebo responses (Stewart-Williams & Podd, 2004). A placebo is an inert substance, routine, or intervention, which contains no specific ingredient that could generate a positive result (Ross & Olson, 1981). However, a placebo is linked to the person's implicit or explicit expectations or beliefs that there is a causal connection between the placebo and the desired result. It is proposed that this belief activates neuropsychobiological mechanisms in the brain that initiate and also mediate the surfacing of an anticipated result (Benedetti & Amanzio, 2013; Benedetti, Mayberg, Wager, Stohler, & Zubieta, 2005).

Placebos are primarily used in medical and pharmacological research to control for so-called non-specific components (e.g. spontaneous improvement, regression to the mean, placebo reaction) of the effects of intervention. Beyond medicine, however, placebo effects were also noted in sports and physical activity, alcohol, and caffeine consumption (Beedie, 2007; Beedie, Stuart, Damian, & Foad, 2006; Dawkins, Shahzad, Ahmed, & Edmonds, 2011; Pollo, Carlino, & Benedetti, 2011; Testa et al., 2006).

In sports, placebos tend to increase one's performance. A meta-analysis of 14 studies revealed a homogeneous variance weighted mean effect size of .31 (Bérdi, Köteles, Szabó, & Bárdos, 2011). In line with Szabo (Szabo, 2013), a more recent meta-analysis, based on nine relevant studies that investigated the psychological effects of training, concluded that about half of the psychological benefits can be linked to placebo effects (Lindheimer, O'Connor, & Dishman, 2015). Thus placebos may be conceived as psychological aids in sports and exercise. Two relatively recent surveys show that 53% of the athletes are ready to accept an unknown, but legitimate product from their coaches, and 67% of them would not mind a placebo-related deception if that had a positive effect on their sport performance (Bérdi, Köteles, Hevesi, Bárdos, & Szabo, 2015). Most (90%) of the elite sports coaches are aware of the placebo effects and at least 44% of them may adopt a placebo with her/his athlete regularly (Szabo & Müller, 2016).

To date, in controlled exercise settings the placebo response has received only little attention. Wright and colleagues found that runners' performance increased by 6.5%, and that slower runners showed a stronger placebo effect after ingesting purported nutritional ergogenic aids (Wright et al., 2009). In another study, the impact of placebo-caffeine on resistance exercise to failure was examined with the participation of 12 men (Duncan, Lyons, & Hankey, 2009). Exercise performance was better when the participants believed that they have ingested real caffeine. Another study of 12 men, drinking either plain water (control), or a labelled performance enhancer drink (placebo), or fatigue inducing (nocebo) drink, manifested a modest placebo effect in a peak minute power incremental arm crank exercise (Bottoms, Buscombe, & Nicholettos, 2014).

The ergogenic effects of creatine monohydrate supplementation are supported and also contradicted by hundreds of studies (Bemben & Lamont, 2005; Demant & Rhodes, 1999; Kreider, 2003; Williams & Branch, 1998). Short term supplementation (e.g. 20 gr/day for 5–7 days) could increase the total muscle creatine content by up to 30% as well as phosphocreatine reserves by up to 40%. and, therefore, it may affect performance in high-intensity, short-duration exercise, which are dependent primarily on phosphocreatine. As for enhancing performance in exercise tasks that are dependent on anaerobic metabolism, additional research is warranted (Williams & Branch, 1998). The effect of an isolated single dose of creatine on anaerobic exercise performance has not been not studied to date. According to our current understanding of the physiology of muscular metabolism, if such effects occur, they could likely be ascribed to a placebo response. To address this problem in a methodologically appropriate manner, a three-group design is needed. Comparison of an intervention group receiving a single dose of creatine and a placebo group might shed light on a pharmacological effect, while the difference between the placebo and and a no-intervention group enables us to measure the placebo effect (Beedie, 2007; Ernst & Reschl, 1995).

Methods

Participants

Participants were physically active undergraduate university students studying in a sports department. After obtaining ethical clearance from the internal Research Ethics Board, we recruited volunteers through campus wide advertisements. A total of 79 undergraduates have volunteered to participate. They all read and signed a written informed consent form. Following baseline measurements, they were randomly assigned to one of three groups: a) intervention group receiving 80 mg/kg creatine monohydrate (n = 26), b) a placebo group receiving starch powder (administered as creatine monohydrate) (n = 26), and c) a water drinking control group (n = 27). Participants' mean age was 19.94 (SD = 1.92) years and 35.4% of them were men. Their mean weight was 65.17 (SD = 10.96) kg, mean height was 171.62 (SD = 8.82) cm. There was statistically no significant difference in the weight and height of the three groups.

Materials

Creatine and its placebo. The recommended daily dose (80 mg/kg) of commercially available creatine monohydrate (Scitec Nutrition® 100% Creatine Monohydrate) was diluted in 4 dl of drinking water. The placebo drink - offered as creatine - contained an identical amount (80 mg/kg) of corn starch powder diluted in 4 dl of drinking water. For the no-intervention control group, 4 dl of drinking water was provided.

Questionnaires. Questionnaires were employed to assess pre-exercise 1) motivation to cooperate in the experiment ((a 6-item scale to control for the cooperation bias of participants) (Szemerszky, Köteles, Lihi, & Bárdos, 2010), 2) expectation regarding performance in the second test-exercise compared to the baseline exercise (one item rated on a 7-point Likert scale), and 3) the perceived performance after the intervention as compared to baseline (one item rated on a 7-point Likert scale).

Anaerobic Step Test. This test relies on a combination of the phosphagen and lactic acid systems and measures the anaerobic capacity. The step platform adopted for exercise purposes was 40 cm high. After the warm up, the subject was standing alongside the bench. The preferred leg rested on top of the bench and it was straightened during the test with each step. The free leg dangled in straight position during the ascent, and its heel reached the height of the bench. The arms were only used for balance. There was a two-count cadence: "one" was up and "two" was down. The duration of the test was one minute. Participants had to go as fast as possible, because the total number of steps in one minute was the final index of performance. Test-retest reliability is high (r>.90), but the persistently noticed significantly higher scores on the second trial indicating dominant- and non-dominant leg differences, as well as learning effects (Beam & Adams, 2011).

Procedure

Upon entering the laboratory, participants were informed about the test procedure and invited to take the one-minute anaerobic step test. The results of this first test were adopted for baseline measure. Next, participants answered the question about their expectations and motivation to cooperate, and received suggestive written information about the postulated beneficial effects of creatine monohydrate on sports performance (the script is available upon request). Subsequently, participants drunk either 4 dl water (control), or corn starch dilution (placebo), or creatine dilution. The intervention was double-blinded, i.e., neither the participants, nor the experimenter was aware of the actual intervention. After a 40-minute rest, participants repeated the same step test with the other leg. Following the intervention, participants indicated the extent to which they perceived that their performance has improved during the second test in comparison to the first test.

Results

Descriptive statistics are presented in Table 1. Overall, two thirds of the participants believed that their performance would improve in the actual test-exercise.

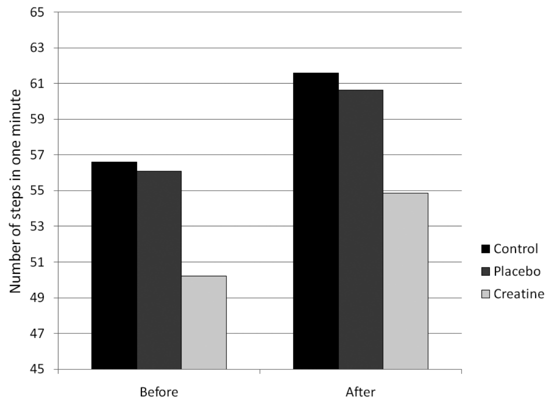
Table 1. Means and standard deviations of four dependent measures in three groups.

Variables	*Creatine-ingesting*	*Placebo-ingesting*	*Controll*
Motivation to cooperate	29.24 (1.16)	27.58 (2.40)	26.17 (3.13)
Expected change performance	5.24 (1.27)	4.85 (0.97)	4.52 (1.28)
Perceived change in performance	3.76 (0.66)	3.42 (0.99)	3.52 (1.04)
Actual change in performance	4.36 (6.34)	4.58 (8.68)	6.22 (8.84)

First the questionnaire data were analyzed with a 3 (group) by 3 (dependent measures: expectation, perceived change in performance, and motivation to cooperate) multivariate analysis of variance (MANOVA). This test yielded a statistically significant multivariate main effect (Pillai' trace = .274, F (6,140) = 3.71, p = .002, $\eta 2p$= .137). The follow-up univariate tests indicated that only motivation to cooperate in the study differed statistically significantly between the groups (F (2, 71) = 10.25, p< .001, $\eta 2p$ = .224). Bonferroni post-hoc tests indicated that the creatine monohydrate group scored higher on motivation to cooperate (M = 29.26; SD = 1.16) than the placebo (M = 27.58; SD = 2.40; effect size (Cohen's d) = 0.90) and than the control group (M = 26,17; SD = 3.13; d = 1.28).

Second, actual change in performance (i.e. the differences in the number of steps performed in the first and the second test) was tested with a group (3) by time (2) mixed analysis of variance using the motivation to cooperate scores as a covariate. This test did not yield a significant group by time interaction (F(1,75) = 0.09, p > .05), or a statistically significant main effectt (F(1,75) = 0.52, p> .05; Figure 1).

Figure 1. Mean number of steps at baseline (Before) and during the one minute step test (After). Although the mean values appear to be higher in all instances during the second test, using motivation to cooperate in the study as a covariate, these differences become statistically not significant.



Third, following the group-level comparisons, individual connections between expectations and actual and perceived change in performance were estimated using correlation analysis. A significant correlation between actual and perceived change in performance (r = .552, p< .001), and between expectation score and perceived change in performance (r = .318, p = .006) were found. The correlation between expectations and actual change in performance was not significant (r = .028, p> .05).

Discussion

The results of this laboratory investigation show that a single dose of creatine monohydrate, or its placebo, do not augment actual physical performance in a brief anaerobic exercise. Concerning perceived performance, group-level comparison showed no differences, however, it was connected with expectations at the individual level. Taken together, participants' expectations did affect perceived performance (i.e. they evoked a subjective placebo effect), but they were not connected with the experimental intervention.

As for the lack of non-specific (placebo) effects, one explanation is that the duration of anaerobic exercise tests are too short to generate an objective placebo effect. It is conjectured that a placebo effect is more likely to surface in longer duration exercise performances (Wright et al., 2009). Another explanation is that participation in a non-competitive and low-subjective-importance laboratory exercise may not be sufficiently challenging to evoke strong expectations which can trigger an objective placebo effect. There was no statistical difference in expectations among the three groups, which means that the creatine and placebo ingestion, and the suggestive written information did not evoke expectations regarding the efficiency of creatine in performance-enhancement. Expectancies were only self-challenges to perform better in a second trial being closer to the topics of personal goal setting and performance motivation that placebos. Still, these personally set expectations were able to shape (or bias) participants' perceived performance.

In the recent past, a "technical" revolution occurred in sports, which has changed the athletes' view on the training aids. According to media information top performance is paired with the adoption of sophisticated aids (e.g., functional food and drinks, magnetic bracelets, kinesiotapes) and monitoring devices (Köteles, Dömötör, Berkes, & Szemerszky, 2015). In placebo-controlled research, these aids and devices usually are not more efficient than their respective placebos, and their effects are not supported by empirical work (Broatch, Petersen, & Bishop, 2014; Chang et al., 2013; Heneghan et al., 2012; Sawkins, Refshauge, Kilbreath, & Raymond, 2007; Vercelli, Ferriero, Bravini, & Sartorio, 2013). However, it is known from empirical research that the placebo effects can enhance sports performance (Beedie & Foad, 2009; Bérdi et al., 2011). Therefore, these aids and devices could mobilize one's mental resources which could translate into better sport or exercise performance. Nevertheless, there should be a powerful belief - or even convincement - to observe a placebo effect.

Conclusions

This double-blind placebo-controlled laboratory study revealed that the ingestion of an isolated single dose of creatine monohydrate before a short anaerobic challenge did not affect neither specific (actual) or non-specific (placebo) exercise performance. However, perceived performance was linked to expectations regarding performance on the second test. However, these expectations were not attributed to the effect of creatine. It is likely that in a low-challenge (and low-subjective-importance) artificial research condition, sufficient expectations cannot be evoked and due to the lack of agent-related expectations placebo effects may not surface.

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