Acute Effects of D- and L-Beta-Hydroxybutyrate on Vigilance (Sustained Attention and Reaction Speed) in Healthy Adults: A Randomized, Double-Blind, Placebo-Controlled Trial

Lia Jiannine[1], Catherine Holen[1], Jose Antonio[1]

[1]Department of Health and Human Performance, Nova Southeastern University, Davie, FL, USA

ABSTRACT

Jiannine L, Holen C, Antonio J. This study evaluated whether a low dose, acute ingestion of beta-hydroxybutyrate (D-BHB) or L-BHB influences vigilance (i.e., sustained attention, reaction speed), fine motor control, memory, mood, or strength in fasted, non–keto-adapted healthy adults. A total of 136 participants (20.5 ± 1.4 years; 70.2 ± 15.6 kg) were randomized into 3 Groups: D-BHB (n = 47), L-BHB (n = 46), or placebo (n = 43). Measures included the Psychomotor Vigilance Test (PVT reaction time) and handgrip strength (mean and peak). Assessments were conducted at baseline and 60 minutes post-consumption. The data were analyzed using a two-way ANOVA with *post hoc* Tukey Tests where appropriate. An exploratory analysis was also conducted to assess within-group changes over time and to estimate effect sizes. A significant group effect was found for reaction time (P = 0.033). Group B (L-BHB) performed significantly faster than placebo (P = 0.029). No time or interaction effects we noted. Lapse counts were higher in the Placebo Group compared to both BHB Groups (P = 0.004). The ANOVA did not show a significant group × time interaction. The main study effect was that both BHB Groups (D- and L-) had fewer lapses overall compared to the Placebo Group, regardless of time point. In the absence of significant time effects (all P > .05), exploratory analyses were conducted to assess within-group changes over time and to estimate effect sizes. Although the ANOVA did not identify statistically significant effects, within-group paired *t*-tests and effect size, estimates were computed to explore potential patterns. These small effect sizes (Group A: 0.264; Group B: 0.271) suggest small changes within Group A and Group B between the pre- and post-60-minute time points. Significant Group differences were found for peak (P = 0.016) handgrip strength. *Post-hoc* tests revealed that Group A (D-BHB) significantly outperformed Group B (L-BHB), while Group C (the Placebo) did not differ from either. Also, an effect size calculation showed a small improvement in both Group A and Group B, with no change in Group C. Thus, the acute ingestion of BHB, particularly the L-isomer, shows a trend towards improved psychomotor attention and reaction time compared to the Placebo Group. Handgrip performance also differed by Group, with the D-BHB Group showing greater strength than the L-BHB Group. There were no significant differences observed on group x time effects. The findings indicate that acute BHB ingestion, particularly the L-BHB, improved reaction speed and reduced attentional lapses compared to the placebo, even at a low 2 g dose. While handgrip strength differed between BHB isomers, neither outperformed the placebo over time. Overall, the data suggests potential cognitive benefits of exogenous BHB on sustained attention at low doses, which supports the need for further dose-response and mechanistic research.

Key Words: Handgrip Strength, Ketone, Performance, Psychomotor Vigilance

INTRODUCTION

Beta-hydroxybutyrate (BHB), a primary ketone body produced during fasting, ketogenic diets, or supplementation acts as an alternative brain fuel and modulates neuroinflammation, synaptic plasticity, and neuroprotection. Most research demonstrates cognitive improvements in animal models of neurodegeneration, metabolic stress, or brain injury, with emerging but mixed evidence in humans (4-6,9,11).

Prior research has focused largely on endurance exercise or metabolic parameters, often in fasted or carbohydrate-restricted states (2,3). Few studies have directly compared the acute effects of BHB isomers on neurocognitive and neuromuscular function in a non-fasted, healthy population. Moreover, the physiological uptake and utilization of the D- and L-isomers are not well understood. D-BHB is the main form produced during fasting, ketogenic diets, and prolonged exercise; whereas, L-BHB is produced in much smaller amounts, is less favored for oxidation, but may have unique neuroprotective roles (1,10) as a signaling molecule.

This study investigates the acute effects of D-BHB and L-BHB supplementation, compared to placebo, on psychomotor vigilance and handgrip strength in healthy young adults. By incorporating both cognitive and neuromuscular indices and analyzing group- and time-dependent effects, the study aims to clarify whether exogenous BHB provides pragmatic benefits.

METHODS

Subjects

The study protocol and consent procedures complied with the Declaration of Helsinki. The participants were informed of their rights, the purpose, methods, risks, and benefits of the research, and they were told that their participation was voluntary and that they could withdraw at any time without reprisal. The protocol was approved by the university IRB (2025-304).

A randomized, double-blind, placebo-controlled design was used to assess the effects of acute BHB supplementation on indices of performance. Healthy men and women (N = 136; D-BHB: n = 47, L-BHB: n = 46, Placebo: n = 43) participated in this study. The participants were randomly assigned to receive a single 2 g dose of D-BHB, L-BHB, or a placebo. Baseline assessments included anthropometric measures, psychomotor vigilance (PVT), and handgrip strength. After baseline characteristics were assessed, the subjects consumed one of the 3 drinks provided (i.e., D-BHB, L-BHB, or placebo). At 60 minutes post-consumption, the following assessments were repeated.

- **Psychomotor Vigilance Test (PVT):** Participants completed a computerized test of sustained attention and alertness at baseline and 60 minutes post-supplementation. During the PVT, participants are instructed to respond as quickly as possible to a visual stimulus (i.e., a number) that appears on a screen at random intervals over a designated period, often five minutes. Each appearance of the stimulus is brief and unpredictable, and the primary data collected are the reaction times.

- **Handgrip Strength:** Peak handgrip strength was measured via a calibrated dynamometer at baseline and follow-ups. Each subject was standing, with the elbow at 90 degrees, and was instructed to squeeze the dynamometer maximally. They were allowed 3 attempts.

Statistical Analysis

The data were analyzed using Python (Statsmodels and SciPy libraries). A two-way ANOVA was conducted to evaluate the effects of Group (A, B, C; between-subjects factor) and Time (Pre, Post60; within-subjects factor) on psychomotor vigilance reaction time. Prior to analysis, the data were screened for normality using the Shapiro-Wilk Test and homogeneity of variance using the Levene's Test; all assumptions were met. The two-way ANOVA assessed the Main effect of Group, the Main effect of Time, and Group × Time interaction. In the absence of significant effects (all $P > .05$), exploratory analyses were conducted to assess within-group changes over time and to estimate effect sizes.

In this study, the Group × Time interaction tested whether changes from baseline to 60 minutes differed between the placebo Group, the D-BHB Group, and the L-BHB Group. A significant interaction would have indicated that one supplement produced a unique improvement over time compared to the others. Although no Group × Time interactions were found for attention, reaction time, or handgrip strength, the overall group differences showed meaningful patterns, such as faster reaction speed in the L-BHB Group and fewer lapses in both BHB Groups. Because these patterns did not appear in the interaction term, we conducted additional exploratory analyses that included within-group paired *t*-tests and effect size estimates to better understand the direction and magnitude of these changes. Paired *t*-tests were performed within each group to evaluate Pre vs. Post60 changes. Effect sizes (Cohen's *d*) were calculated for within-group (paired) and between-group (independent) comparisons to quantify the magnitude of differences, even in the absence of statistical significance. Descriptive trends were visualized using reaction time profiles across the Groups and timepoints to support interpretation of potential group-level patterns. All analyses used a significance level of $\alpha = 0.05$.

RESULTS

The participants' baseline characteristics showed no significant Group differences (see Table 1).

Table 1. Subject Characteristics.

	Group A D-BHB (n = 47)	Group B L-BHB (n = 46)	Group C Placebo (n = 43)
Age (yrs)	20.7 ± 2.0	20.5 ± 1.2	20.3 ± 1.0
Height (m)	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1
Weight (kg)	70.1 ± 15.3	69.8 ± 17.0	70.6 ± 14.3
BMI	24.5 ± 4.7	24.3 ± 3.6	23.8 ± 2.7

The data are expressed as the mean ± SD. Legend: **BMI** = Body Mass Index (weight/height^2), **kg** = Kilograms, **m** = Meters, yrs = Years. An unpaired *t*-test revealed no significant differences between the Groups. Group A (21 males and 25 females); Group B (24 males and 22 females); Group C (22 males and 22 females).

Psychomotor Vigilance (Attention and Reaction Time)

A two-way analysis of variance (ANOVA) was conducted to examine the effects of Group (A, B, and C) and Time (Pre vs. Post60) on psychomotor vigilance reaction time. The results revealed no significant main effect of Group, $F(2, 266) = 1.99$, P = .138, and no significant main effect of Time, $F(1, 266) = 0.94$, P = .333. Furthermore, the Group × Time interaction was not significant, $F(2, 266) = 0.44$, P = .647. Assumptions of normality and homogeneity of variance were met (i.e., the Shapiro-Wilk Test indicated no significant deviations from normality (P > .05), and the Levene's Test confirmed equal variances at both time points (Pre: P = .22; Post60: P = .13).

Exploratory Analysis: Within-Group Comparisons and Effect Sizes

Although the ANOVA did not identify statistically significant effects, within-group paired *t*-tests and effect size estimates were computed to explore potential patterns. These small effect sizes suggest minor changes within each Group between Pre and Post 60-min time points (Table 2 and Figure 1).

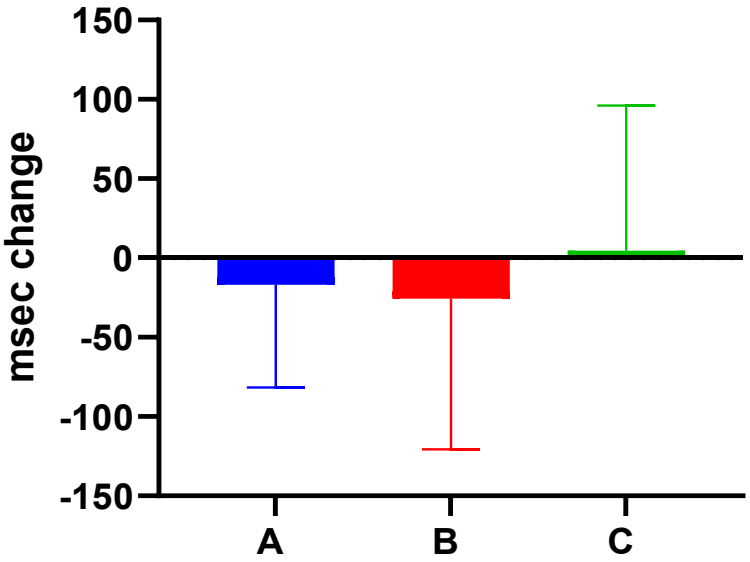
Table 2. Psychomotor Vigilance Test (PVT) – Reaction Time.

	Group A D-BHB (n = 47)	Group B L-BHB (n = 46)	Group C Placebo (n = 43)
RT Pre (msec)	412 ± 92	397 ± 138	415 ± 128
RT 60-min	395 ± 85	371 ± 7	419 ± 136
Cohen's d	-0.264	-0.271	0.051
P value	0.077	0.073	0.738

The data are expressed as the mean ± SD. Legend: **msec** = milliseconds.

TIME EFFECTS (Pre vs. Post60)

Figure 1. Psychomotor Vigilance (Attention and Reaction Time). The data are presented as the mean and standard deviation. Groups A and B improved similarly (d ≈ -0.27; small effect size); Group C showed no change.



	A	B	C
Mean	-17.00	-25.72	4.721
Std. Deviation	64.61	94.86	91.38
Std. Error of Mean	9.424	13.99	13.94

Table 3 shows that there were no effects of the treatment on handgrip strength.

Table 3. Peak Handgrip Strength.

	Group A D-BHB (n = 47)	Group B L-BHB (n = 46)	Group C Placebo (n = 43)
Pre	37 ± 10	41 ± 16	37 ± 14
60-min	38 ± 10	44 ± 17	40 ± 13
Delta	1 ± 5	3 ± 7	3 ± 7

The data are expressed as the mean ± SD. Legend: **msec** = milliseconds.

Although Group B showed significantly higher strength than Group A overall (P = 0.048), Group B did not reach significance in overall strength from Groups A and C. Also, there was no significant Time × Group interaction (P = 0.215) or an effect of Time (P = 0.229).

CONCLUSIONS

This study employed a challenging design for detecting nutritional effects of a single, low 2-gram acute dose administered to healthy, fasted, and non-keto-adapted adults, which is a population that measurable cognitive or performance shifts are typically difficult to detect. Exploratory within-group analyses reveal small but consistent improvements for both the D-BHB and the L-BHB Groups with no changes in the Placebo Group. Collectively, these results highlight that exogenous BHB, especially the L-isomer condition that may enhance aspects of attention and reaction performance under acute, low-

dose conditions. Future research should examine longer treatment durations, higher dosages, and perhaps different populations.

ACKNOWLEDGEMENTS

We would like to thank the International Society of Sports Nutrition and Ketone Labs for their support of this project.

Address for correspondence: Jose Antonio PhD, Department of Health and Human Performance, NSU Florida, Davie FL USA. Email: Jose.Antonio@nova.edu

References

1. Cuenoud B, Hartweg M, Godin J, et al. Metabolism of exogenous D-beta-hydroxybutyrate, an energy substrate avidly consumed by the heart and kidney. ***Front Nutr.*** 2020;(7), (Online). doi:10.3389/fnut.2020.00013.

2. Evans M, McClure T, Koutnik A, et al. Exogenous ketone supplements in athletic contexts: Past, present, and future. ***Sports Med.*** 2022;(52):25-67, (Online). doi:10.1007/s40279-022-01756-2.

3. Quinones M, Weiman K, Lemon P. Ketone monoester followed by carbohydrate ingestion after glycogen-lowering exercise does not improve subsequent endurance cycle time trial performance. ***Nutr.*** 2024;(16), (Online). doi:10.3390/nu16070932.

4. Reger MA, Henderson ST, Hale C, et al. Effects of beta-hydroxybutyrate on cognition in memory-impaired adults. ***Neurobiol Aging.*** 2004;(25):311-314.

5. Rojas R, Griñán-Ferré C, Castellanos A, et al. Beta-hydroxybutyrate counteracts the deleterious effects of a saturated high-fat diet on synaptic AMPAR receptors and cognitive performance. ***Mol Metab.*** 2025;99:(Online). doi:10.1016/j.molmet.2025.102207.

6. Shabbir I, Liu K, Riaz B, et al. Investigating the therapeutic potential of the ketogenic diet in modulating neurodegenerative pathophysiology: An interdisciplinary approach. ***Nutr.*** 2025;17: (Online). doi:10.3390/nu17071268.

7. Waldman H, O'Neal E, Barker G, et al. A ketone monoester with carbohydrate improves cognitive measures postexercise, but not performance in trained females. ***Med Sci Sports Exerc.*** 2023;(56):725-736, (Online). doi:10.1249/mss.0000000000003352.

8. Waldman H, O'Neal E, Barker G, et al. No benefit of ingesting a low-dose ketone monoester supplement on markers of cognitive performance in females. ***J Cogn Enhanc.*** 2023;(7):193-202, (Online). doi:10.1007/s41465-023-00275-w.

9. Wu Y, Gong Y, Luan, Y, et al. BHBA treatment improves cognitive function by targeting pleiotropic mechanisms in transgenic mouse model of Alzheimer's disease. ***FASEB J.*** 2019; (34):1412-1429, (Online). doi:10.1096/fj.201901984r.

10. Yao A, Li Z, Lyu J, et al. On the nutritional and therapeutic effects of ketone body D-beta-hydroxybutyrate. ***Appl Microbiol Biotechnol.*** 2021;(105):6229-6243, (Online). doi:10.1007/s00253-021-11482-w.

11. Yu Q, Wong K-K, Lei O-K, et al. Acute ketone monoester supplementation in young adults: Modulating metabolic and neurocognitive functions across body weights. ***Appl Physiol Nutr Metab.*** 2024:2024-0229, (Online). doi:10.1139/apnm-2024-0229.