

Exogenous Ketosis Increases D-β-Hydroxybutyrate Concentrations in Human Cerebrospinal Fluid

Simon K. Kjær ^{1,2}, Jens H. Voigt ^{1,2}, Julie Bondgaard ^{1,2}, Nikolaj Rittig ^{1,2,3}, Niels Møller ^{1,4,2}, Jakob Hansen ⁵, and Mads Svart ^{1,2,3}

Received: 28 February 2025

Accepted: 12 March 2025

Published: 19 November 2025

¹ Steno Diabetes Center Aarhus, Aarhus University Hospital, Denmark

² Department of Clinical Medicine, Aarhus University, Denmark

³ Department of Internal Medicine, Regional Hospital Horsens, Denmark

⁴ Department of Endocrinology and Internal Medicine, Aarhus University Hospital, Denmark

⁵ Department of Forensic Medicine, Aarhus University, Aarhus, Denmark

Correspondence

Simon K. Kjær

Steno Diabetes Center Aarhus, Aarhus University Hospital, Denmark

simkjr@clin.au.dk

Abstract

Over the last decade, there has been growing interest in the use of ketone supplements to explore their effects on elite-level cycling performance, training adaptations, and, in particular, recovery. This includes areas related to the brain, such as enhancing cognitive resilience post-exercise, improving sleep quality and efficiency, and increasing the neuroprotective hormone brain-derived neurotrophic factor (BDNF) and dopamine levels in circulation. We hypothesized that ketone ester intake before a planned lumbar puncture would increase D-β-hydroxybutyrate (βHB) and subsequently BDNF and dopamine in the cerebrospinal fluid (CSF), a reflection of the levels in the brain. In a randomized, placebo-controlled, single-blind, parallel-group study, patients referred for elective lumbar puncture received either 30 g of ketone ester 1 hour before (KET 1H), 2 hours before (KET 2H), or a placebo (PLA) before the lumbar puncture procedure. βHB concentrations were measured using point-of-care testing (POCT) and Liquid Chromatography-Mass Spectrometry (LC-MS). The primary endpoint was βHB concentrations in the CSF. The study is ongoing; as of submission, 20 out of 24 patients have been included: 6 in PLA, 7 in KET 1H, and 7 in KET 2H. Blood βHB concentrations, measured by POCT, averaged 0.2 ± 0.09 in PLA, 3.22 ± 0.85 in KET 1H, and 2.66 ± 1.01 in KET 2H following lumbar puncture. CSF βHB, also measured by POCT, was 0.05 ± 0.05 in PLA and increased to 0.17 ± 0.08 ($P = 0.07$) in KET 1H and to 0.47 ± 0.17 ($P < 0.001$) in KET 2H. In conclusion, KE treatment administered 2 hours before lumbar puncture was associated with the highest increase in βHB levels in CSF compared to placebo. Verification by LC-MS and neurotransmitter measurements will follow upon study completion. Our results suggest a delay in the passage of βHB from blood into the CSF, which underlines the importance of timing ketone supplement ingestion to maximize its effects on the central nervous system in the context of exercise and recovery.

Keywords

ketosis; cerebrospinal fluid; physiology



This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



