Proceedings of the Nutrition Society (2023), **82 (OCE5)**, E316 doi:10.1017/S0029665123004159

Summer Conference 2023, 3–6 July 2023, Nutrition at key stages of the lifecycle

Cannabidiol (CBD) ingestion increases ad libitum energy intake in healthy adults but does not affect postprandial glucose or lipid metabolism

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The endocannabinoid system has emerged as a potent regulator of energy intake[1], but little is known about the effects of most individual phytocannabinoids on eating behaviour. Cannabidiol (CBD) is legal, non- intoxicating, and has a vast consumer market as well as clinical use in epilepsy treatment. Preclinical research suggests that CBD may reduce energy intake in rodents[2], but no studies have examined its effect in humans. Therefore, the primary aim of this study was to examine whether acute CBD ingestion affected ad libitum energy intake in healthy adults, whilst secondary outcomes were whether CBD altered the hormonal or metabolic responses to a mixed-macronutrient meal.

Fifteen healthy volunteers (11 males; age 25 ± 5 years; body mass index 24.3 ± 3.0 kg/m^2) completed two conditions in a double-blind, randomised, counterbalanced crossover study. Participants ingested CBD (300 mg) or placebo and consumed a mixed-macronutrient shake 30 minutes later. Postprandial metabolism was then assessed over 2.5 hours. Plasma glucose, triglyceride, non-esterified fatty acid, insulin, glucagon-like peptide 1 (GLP-1) and total ghrelin concentrations were quantified using an automated analyser (ABX Pentra c400) and enzyme-linked immunoassays. Energy intake was assessed via an *ad libitum* pasta lunch 3.25 hours after CBD/placebo ingestion; participants served themselves and ate until 'comfortably full'. Subjective appetite (hunger, fullness, and desire to eat) was assessed hourly via visual analogue scales. Outcomes were compared between conditions using paired t-tests or Wilcoxon Signed-Rank tests, depending on data normality. Plasma concentrations and appetite scores were compared using two-way repeated measures ANOVAs.

Energy intake at lunch was 193 (80, 306; 95%CIs) kcal greater following CBD ingestion (CBD 979 ± 462 kcal; placebo 786 ± 280 kcal; $P = 0.003$; Cohen's d^z=0.94). Subjective appetite did not differ between conditions ($p > 0.05$). Minimum ghrelin concentration was 100 (143, 55) pg/mL less following CBD ingestion ($P = 0.02$), but there was no significant interaction effect for concentrations over time, or between-condition difference in AUC ($P > 0.05$). There were no significant differences or interaction effects for any other blood-based markers ($P > 0.05$).

This was the first study to assess effects of CBD on energy intake in humans, suggesting that CBD may induce hyperphagia. This contradicts research showing that CBD reduced energy intake in rodents[2]. Reasons for this discrepancy are unclear, but further studies are required to replicate present findings and establish whether CBD could have clinical use in this regard. CBD may be preferable, clinically, to tetrahydrocannabinol (THC), which is used to promote energy intake in AIDS-related anorexia, as CBD is non- intoxicating. Mechanistically, the lack of difference in subjective appetite may suggest that satiation was impaired. However, this was not due to increased circulating ghrelin, or decreased GLP-1 concentrations.

Acknowledgments
The authors would like to thank the participants for completing the study.

References

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