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How exercise and a special ketone supplement may improve heart health, metabolism, and brain function

Submission date	Recruitment status	[_] Prospectively registered
27/11/2025	Recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
03/12/2025	Ongoing	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
02/12/2025	Nutritional, Metabolic, Endocrine	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Being overweight or obese can harm both physical and mental health, increasing the risk of heart disease, diabetes, and even cognitive problems. At the same time, spending too much time watching short, fast-paced videos on mobile apps may affect attention and memory. This study aims to find out whether combining exercise (short bursts of high-intensity activity) and a special dietary supplement called exogenous ketones can help improve weight, fitness, and brain health. Researchers also want to see if these strategies can reduce the negative effects of too much short-video viewing.

Who can participate?
Adults aged 18 to 45 can take part. For some parts of the study, participants need to have a body mass index (BMI) of 23 or higher or a body fat percentage of 30% or more. For other parts, there are no weight requirements.

What does the study involve? (for participants)
Participants will do short sprint interval training (SIT) exercises and take ketone supplements. Some sessions will be in normal oxygen conditions, and others in lower oxygen (hypoxic) conditions. Everyone will receive a personalized exercise plan and free long-term advice on diet and fitness.

What are the possible benefits and risks of participating?
Benefits include a detailed report on your body composition, fitness level, and cognitive function. You'll also get tailored exercise and diet guidance. The study does not involve any known risks.

Where is the study run from?
The study is based at the kinesiology lab in the Faculty of Education at the University of Macau, China.

When is the study starting and how long is it expected to run for?
The study began on 16 September 2024 and will run for about two years.

Who is funding the study?
The research is funded by the Multi-Year Research Grant General Research Grant (MYRG-GRG2023 & MYRG-GRG2025) from the Faculty of Education, University of Macau.

Who is the main contact?
The main contact for the study is Dr Jay Lee 405630519@qq.com, supervised by Professor Zhaowei Kong

Contact information

Type(s)
Public, Scientific, Principal investigator

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Study information

Scientific Title
Effects of ketone supplementation and sprint interval training in normoia and hypoxia on cardiometabolic and neurocognitive outcomes in overweight/obese young adults

Study objectives
This research comprises three experiments evaluating the isolated and synergistic effects of exogenous ketone supplementation and brief sprint interval training (SIT) under normoxic versus hypoxic conditions as lifestyle interventions for mitigating multimorbidity in obesity or preventing cognitive impairment in young adults.

The first experiment will determine the acute response to ketone ingestion alongside a single bout of hypoxic compared to normoxic SIT on domains including metabolic factors, cardiovascular function, inflammation, executive function, and brain perfusion. The second experiment will evaluate weight loss, cardiometabolic, and neurocognitive outcomes following a

4-week sustained intervention of ketone supplementation and sprint training carried out in hypoxia versus normoxia. The third experiment will investigate the influence of short videos on cognition and the preventive effects of ketone ingestion and SIT.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 25/06/2025, Sub-Panel on Biomedical Science & Engineering Research Ethics of Panel on Research Ethics the Research Committee of the University of Macau (Room 5011 Administration Building University of Macau, N6 Avenida da Universidade Taipa, Macau, 519000, China; +853 8822 4399; rskto.ethics@um.edu.mo), ref: BSE-0213-2025

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Overweight or obesity

Interventions
For study 1, it utilizes a randomized, counterbalanced, single-blinded crossover design comparing four conditions: non
exercise control (CON), sprint interval training (SIT), exogenous ketone supplement (EKS), and EKS+SIT (EKS-SIT). Participants complete all conditions in both normoxia (approx. 100m) and after acute exposure to 2500m normobaric
hypoxia in an altitude simulation chamber. Participants ingested two servings of either (i) a taste- and volume-matched placebo or (ii) ketone acids (200 mg/kg body weight of ketone in total), at 60 and 30 minutes before exercise. Trails involving SIT consisted of 10 × 6-second “all-out” cycling bouts interspersed with 9 seconds of rest, while non-exercise trials involved time-matched seated rest.

Study 3 is almost identical to Study 1, except that the environment is limited to normoxia and three servings of either (i) a taste- and volume-matched placebo or (ii) ketone acids (200 mg/kg body weight of ketone in total) will be provided. Three servings will be provided 15 min before and 30min and 1 hour after the exercise.

Study 2 employs an 8-arm RCT with participants randomly allocated into 4 matched normoxic groups from Study
1 and 4 identical hypoxic training groups (HYP-CON, HYP-SIT, HYP-EKS, HYP-EKS+SIT) exposed weekly to
normobaric hypoxia simulating 2500m to 4000m elevations. A 2-week lead-in ensures diet and activity stabilization.
Identical pre-post assessments include: cardiorespiratory fitness, body composition, blood biomarkers of metabolism
and appetite, cognitive test battery, and 2-hr oral glucose tolerance testing. During the 4-week

intervention, diets are
required consistent via 3-day food diaries and recalls to support compliance. Heart rate, ratings of perceived exertion
and enjoyment are monitored per training session.

Randomization will be performed at www.randomizer.org

Intervention Type
Supplement

Primary outcome(s)
Study 1
1. Cognitive function is measured using Stroop Test, N-Back, and Delay Discounting Task at baseline and post-intervention
2. Perceived fatigue is measured using Rate of Perceived Exertion (RPE) at pre-exercise, during exercise, and post-exercise
3. Food motivation is measured using Food Craving Questionnaire-State (FCQ-S) at baseline and post-intervention
4. Prefrontal cortex activation patterns are measured using functional Near-Infrared Spectroscopy (fNIRS) during cognitive tasks at baseline and post-intervention
5. Blood glucose, lactate, and beta-hydroxybutyrate are measured using capillary blood sampling analyzed with portable biochemical analyzers at baseline, 45 minutes after the supplement, 60 minutes after the supplement, post-exercise, 1 hour post-exercise, and 2 hours post-exercise
6. Aerobic fitness level is measured using submaximal VO_2 kinetics test with CORTEX METAMAX 3B at baseline, 1 hour post-exercise, 2 hours post-exercise, and 24 hours post-exercise
7. Intervention adherence is measured using blood beta-hydroxybutyrate and lactate concentrations via capillary blood sampling analyzed with portable biochemical analyzers at baseline, 45 minutes after the supplement, 60 minutes after the supplement, post-exercise, 1 hour post-exercise, and 2 hours post-exercise

Study 2
8. Cardiorespiratory fitness is measured using graded exercise test on a cycle ergometer with metabolic cart and heart rate monitoring at baseline and post-intervention
9. Body composition is measured using Dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA) at baseline and post-intervention
10. Blood biomarkers of metabolism and appetite are measured using venous blood sampling analyzed via standard clinical chemistry assays at baseline and post-intervention
11. Cognitive function and prefrontal cortex activation patterns are measured using Stroop Test, N-Back, Delay Discounting Task, and fNIRS monitoring during cognitive tasks at baseline, mid-test, and post-intervention
12. Glucose tolerance is measured using 2-hour Oral Glucose Tolerance Test (OGTT) with venous blood sampling at baseline and post-intervention

Study 3
13. Cognitive function is measured using Stroop Task, N-Back Task, and Go/No-Go Task at baseline and 0, 30, and 60 minutes after intervention
14. Prefrontal cortex activation patterns are measured using fNIRS monitoring during cognitive tasks at baseline and 0, 30, and 60 minutes after intervention
15. Blood glucose is measured using finger-prick with portable glucometer at baseline, pre-exercise, 1 hour post-exercise, 90 minutes post-exercise, and 2 hours post-exercise
16. Blood beta-hydroxybutyrate is measured using finger-prick with portable ketone meter at

baseline, pre-exercise, 1 hour post-exercise, 90 minutes post-exercise, and 2 hours post-exercise
17. Anxiety is measured using Zung Self-Rating Anxiety Scale (SAS) at pre-test
18. Impulsiveness is measured using Barratt Impulsiveness Scale (BIS-11) at baseline and post-intervention
19. Mobile phone addiction tendency is measured using Mobile Phone Addiction Tendency Scale at baseline and post-intervention
20. Short-form video addiction is measured using short version of social networking sites addictive tendency scale at baseline and post-intervention
21. Smartphone addiction is measured using Smartphone Addiction Scale – Short Version (SAS-SV) at baseline and post-intervention
22. Affective responses are measured using visual analog scale (VAS), Feeling Scale (FS), Physical Activity Enjoyment Scale (PACES), and Empirical Valence Scale (EVS) over the whole intervention
23. Heart rate is measured using Polar heart rate monitor (Polar H10) over the whole intervention
24. Step count is measured using ActiGraph accelerometer over the whole intervention

Key secondary outcome(s))

Study 1
1. Body composition distribution is measured using Dual-energy X-ray absorptiometry (DEXA) and anthropometric measurements at baseline
2. Side effects are measured using oral enquiry after supplementation and exercise sessions at after each intervention session
3. Appetite is measured using Food Craving Questionnaire-State (FCQ-S) at baseline and after intervention
4. Dietary behaviors are measured using 24-hour dietary recall, Three-Factor Eating Questionnaire, and Eating Behavior Scale at baseline and after intervention
5. Anxiety is measured using Generalized Anxiety Scale at baseline and after intervention
6. Ratings of perceived exertion (RPE) are measured using Borg Rating of Perceived Exertion Scale at before, during, and after each exercise session
7. Enjoyment is measured using Physical Activity Enjoyment Scale (PACES), Exercise Enjoyment Scale (EES), and Exercise-induced Feeling Inventory (EFI) at immediately after exercise sessions
8. Heart rate is measured using Polar heart rate monitor (Polar H10) at continuously during intervention sessions
9. Blood pressure is measured using automated sphygmomanometer at baseline, 45 minutes after the supplement, 60 minutes after the supplement, post-exercise, 1 hour post-exercise, and 2 hours post-exercise
10. Peripheral oxygen saturation (SpO_2) is measured using pulse oximeter at during intervention sessions

Study 2
11. Dietary compliance is measured using 3-day food diaries and 24-hour dietary recalls analyzed using the “bohejiankang ()” app at one week before the intervention (lead-in period) as baseline and during the 4-week intervention (e.g., weekly)

Study 3
12. Aerobic fitness is measured using maximal oxygen uptake test with Cortex MetaMax 3B metabolic cart during graded exercise test at baseline
13. Smartphone addiction is measured using proposed diagnostic criteria for smartphone addiction at baseline

All studies
14. Background information is measured using oral enquiry including major, age, origin, and date

of birth at baseline for Study 1 and 3 and baseline, during, and after the intervention for Study 2
15. Physical activity is measured using International Physical Activity Questionnaire at baseline for Study 1 and 3 and baseline, during, and after the intervention for Study 2
16. Stature is measured using stadiometer at baseline for Study 1 and 3 and baseline, during, and after the intervention for Study 2

Completion date
31/08/2026

Eligibility

Key inclusion criteria
For study 1 and 2
1. Aged 18-45 years old.
2. BMI≥ 23 kg/m² or percentage of body fat (PBF) ≥ 30%, weight stability (±3 kg in past 6 months).
3. Altitude residence <1000 m, no prior hypoxic training, physically healthy.
4. Right-handed.

Study 3
1. Aged 18-30 years old
2. phone use time ≥ 2 hours/day
3. Right-handed

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
Female

Total final enrolment
0

Key exclusion criteria
Study 1 and 2.
1. Structured training/ diets
2. Medication use (oral contraceptive or any medication intake)
3. Smoking/alcohol use

4. Exercise limitations
5. Medical conditions (endocrine, metabolic, cardiovascular respiratory issues)
6. Unable to provide the signed informed consent.
7. Any diseases within the past year

Study 3.
1. Medication use (oral contraceptive or any medication intake)
2. Smoking/alcohol use
3. Exercise limitations
4. Medical conditions (endocrine, metabolic, cardiovascular respiratory issues)
5. Unable to provide the signed informed consent.
6. Any diseases within the past year
7. Structured exercise training

Date of first enrolment
16/09/2024

Date of final enrolment
01/06/2026

Locations

Countries of recruitment
China

Macao

Study participating centre
Kinesiology lab
Room 3014, N8 Sports Complex, University of Macau
Macau
China
519000

Sponsor information

Organisation
Faculty of Education, University of Macau

Funder(s)

Funder type
Not defined

Funder Name
Faculty of Education, University of Macau

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Jay Lee, with email 405630519@qq.com

IPD sharing plan summary
Available on request