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Effects of guanidinoacetic acid and creatine monohydrate supplementation on markers of health and cognitive function

Submission date
13/11/2025

Recruitment status
No longer recruiting

Registration date
17/11/2025

Overall study status
Completed

Last Edited
20/11/2025

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Creatine monohydrate (CrM) supplementation (e.g., 4 x 5 g or 20 g/d for 5-7 days and 3 – 6 g/d for 4-12 weeks) increases muscle creatine and phosphocreatine (Cr) content by 20% - 40%, and brain creatine and phosphocreatine content by 5% - 15%, thereby improving the ability to produce energy during high-demand states. While most studies have evaluated the effects of CrM supplementation on physical exercise performance several studies have reported that high-dose creatine supplementation can increase brain phosphocreatine content leading to improved cognitive function. Creatine is obtained in gram quantities from meat and fish and is synthesized in the body when dietary availability is low (2 – 4 grams/kg). In over 30 years of research, clinical trials involving creatine monohydrate supplementation have reported no adverse health risks other than a small amount of weight and muscle mass gain (a desired effect). Conversely, several health benefits have been reported throughout the lifespan.

Guanidinoacetic Acid (GAA) is a precursor in the natural synthesis of creatine in muscle, the heart, and particularly in the brain. Since some animals more effectively convert GAA to creatine, GAA has been added to the feed of animals consumed by humans (e.g., chickens, pigs, etc.) as a means of increasing muscle mass at EFSA-approved dosages of 1,200 mg/kg/d. GAA has also been used as a nutrient in human nutrition since the 1950s and is sold as an ingredient for dietary supplements. No adverse effects have been reported from GAA supplementation (1.2 – 4.8 grams/day for 4 – 12 weeks), although a non-clinically significant increase (≈ 3.5 µmol/L) in homocysteine levels was reported when supplementing the diet with 4.8 g/d for 4 weeks and although values remained within normal ranges (5 – 20 µmol/L) and were well below values considered to be high risk (> 50 µmol/L). Since GAA supplementation has been reported to increase energy levels in the brain more effectively than CrM, dietary supplementation with GAA (with and without CrM) may be an effective way to improve cognitive function. For this reason, GAA supplementation has been suggested to be a novel nootropic to improve cognitive function and brain health. However, while there is strong theoretical rationale, the effects of GAA supplementation (with or without CrM supplementation) on cognitive function have not been studied, particularly in active aging populations who may benefit.

The purpose of this study is to evaluate the effects of GAA supplementation with and without CrM on markers of cognitive function and health markers in older adults.

Who can participate?
Healthy adult volunteers aged between the ages of 45 and 75 years.

What does the study involve?
Participants will be randomly assigned to one of three groups. All groups will follow the same exercise and diet program, but the supplements will differ:

Group 1: Placebo for both GAA and CrM.
Group 2: GAA supplement plus a placebo for CrM.
Group 3: GAA supplement plus CrM supplement.

The supplements (or placebos) will be provided in stick packs for double-blind administration. Participants will take two doses per day, one with breakfast and one with dinner, for 12 weeks.

What are the possible benefits and risks of participating?
Possible benefits of participating include increased insight into one's health and fitness status (i.e., anthropometric measurements, vital sign measurements, lab values, DXA body composition and bone density values, etc.). Possible risks of participation include complications from the blood draws (i.e., pain, dizziness, nausea, etc.), radiation exposure from the DXA scan (< 1 mRem per scan), side effects of the supplements (i.e., bloating, cramping, diarrhea, etc.), and possible allergic reactions to the supplements.

Where is the study run from?
WoodNext Foundation, USA.

When is the study starting and how long is it expected to run for?
September 2025 to June 2026.

Who is funding the study?
WoodNext Foundation, USA.

Who is the main contact?
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Contact information

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Study information

Scientific Title
Effects of 12 weeks of guanidinoacetic acid and creatine monohydrate supplementation during an exercise and diet intervention on markers of health and cognitive function in older adults

Study objectives
The objective of this study is to evaluate the effects of GAA supplementation with and without CrM on markers of cognitive function and markers of health in older adults.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/02/2025, Texas A&M University Institutional Review Board (IRB) (301 Old Main Drive Suite 3104, College Station, 77845, United States of America; +1 9798458585; irb@tamu.edu), ref: STUDY2025-1539

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Parallel

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Guanidinoacetic Acid (GAA) supplementation with and without Creatine Monohydrate (CrM) on markers of cognitive function and health in older adults.

Interventions
Participants will be randomized (using Stratified Randomization using sealed envelopes) into one of the three treatment groups listed below.

Treatment 1. Exercise/Diet + Guanidinoacetic Acid Placebo (2 x 1 g/d maltodextrin) + CrM Placebo (2 x 5 g/d maltodextrin); Treatment 2. Exercise/Diet + Guanidinoacetic Acid (2 x 1 g/d) + Placebo (2 x 5 g/d maltodextrin);
Treatment 3. Exercise/Diet + Guanidinoacetic Acid (2 x 1 g/d) + Creatine Monohydrate (2 x 5 g/d).

The GAA, CrM and placebo (maltodextrin) supplements will be prepared in labeled stick packs for double-blind administration by the Sponsor. Participants will be asked to consume the first supplement dose with breakfast and the second supplement dose with dinner for 12-weeks.

Intervention Type
Supplement

Primary outcome(s)
1. Body weight (kg) measured using Calibrated digital scale at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

2. Body fat mass (kg) measured using calibrated DXA at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

3. Body percent body fat (%) measured using calibrated DXA at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

4. Waist-to-Hip Circumference (W/H) measured using tension regulated tape measure at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

5. Cognitive Function measured using COMPASS cognitive function test battery at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

Key secondary outcome(s)

1. Resting Energy Expenditure (REE) measured using ParvoMedics TrueOne 2400 metabolic cart at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

2. Aerobic capacity (GXT) measured using ParvoMedics TrueOne 2400 metabolic cart at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

3. Muscular strength (1 RM) measured using Nebula bench press and leg press at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

4. Muscular endurance (repetitions at 70% 1RM) measured using Nebula bench press and leg press at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

5. Lipid panel measured using calibrated and automated analyzer at Clinical Pathology Laboratory (CPL) at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

6. Comprehensive metabolic panel (Chem Panel) measured using calibrated and automated analyzer at Clinical Pathology Laboratory (CPL) at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

7. Complete Blood Count (CBC) with automated differential measured using calibrated and automated analyzer at Clinical Pathology Laboratory (CPL) at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

8. Hemoglobin A1c (HbA1c) measured using calibrated and automated analyzer at Clinical Pathology Laboratory (CPL) at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

9. Quality of Life (QOL) measured using SF-36 Quality of Life (QOL) questionnaire at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

10. Side-effects measured using a side-effects questionnaire at 0 weeks (baseline), 6 weeks (1st follow-up), 12 weeks (2nd follow-up)

Completion date
08/06/2026

Eligibility

Key inclusion criteria
1. Male or female between the ages of 45 and 75 years.
2. Participant is willing to comply with the study procedures.
3. Participant is willing to refrain from alcohol intake and use of non-steroidal anti-inflammatory drugs (NSAIDS), aspirin, and other over-the-counter (OTC) pain medications for 48-hours prior to each testing session.
4. Participant is willing to complete the study based on the duration of the individual visits and scheduling requirements.
5. Participant is willing to comply and understand the cognitive function tests.

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
45 Years

Upper age limit
75 Years

Sex
All

Total final enrolment
75

Key exclusion criteria
1. Participant has a known vitamin B12/B6 or folate deficiency.
2. Participant has known homocystinuria.
3. Participant has high homocysteine levels.
4. Participant has a history of kidney disease requiring dialysis.
5. Participant has diagnosed cognitive impairment or neurological disease.
6. Participant is pregnant, breastfeeding, or wishing to become pregnant during the study.
7. Participant has uncontrolled heart disease, hypertension, diabetes, thyroid disease, cancer, neurological disease, or medically treated major psychological or depressive disorder that may affect results of the study.
8. Participant has a known allergy to meat or fish, GAA, CrM, or Maltodextrin.

Date of first enrolment
08/09/2025

Date of final enrolment
08/03/2026

Locations

Countries of recruitment
United States of America

Sponsor information

Organisation
WoodNext Foundation

Funder(s)

Funder type

Funder Name
WoodNext Foundation

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available