ISRCTN68542582 https://doi.org/10.1186/ISRCTN68542582

Effects of guanidinoacetic acid supplementation with and without creatine monohydrate on cognitive function

Submission date
10/11/2025

Recruitment status
No longer recruiting

Registration date
12/11/2025

Overall study status
Completed

Last Edited
14/09/2026

Condition category
Other

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

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. 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 short-term GAA supplementation with and without CrM on markers of cognitive function and health markers.

Who can participate?
We are recruiting up to 100 male and female participants between the ages of 18 and 65 with a goad of completing 60 participants.

What does the study involve?
Each participant will be asked to visit the lab three times over approximately a six week period. Each study visit will last approximately two hours (minus the first study visit or Familiarization which will last approximately one hour). Each visit after the first Familiarization visit will include; anthropometric measures (height and weight), vital signs (HR and BP) measures, blood draw, DXA scan, physical activity questionnaire (IPAQ), quality of life questionnaire (SF-36), profile of mood states questionnaire (POMS), memory complaint questionnaire (MAP-Q), Wechsler memory scale (WMS - VAP1 and VAP2) questionnaire, Mini-Mental State Examination (MMSE), the Leeds sleep evaluation questionnaire, The Cohen's perceived stress scale (PSS), a menstrual status questionnaire (females only), a menopause status questionnaire (females only), COMPASS cognitive test battery, and side-effects assessment.

What are the possible benefits and risks of 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?
The study was run from the Exercise & Sport Nutrition Laboratory (ESNL) at Texas A&M University (USA)

When is the study starting and how long is it expected to run for?
The study planning started on November 20, 2023 and was completed on September 20, 2025.

Who is funding the study?
The study is being funded by the WoodNext Foundation (USA)

Who is the main contact?
Dr Richard Kreider, rbkreider@tamu.edu

Contact information

Type(s)
Scientific, Principal investigator

Contact name
Dr Richard Kreider

ORCID ID
https://orcid.org/0000-0002-3906-1658

Contact details
675 John Kimbrough Blvd.
#118

College Station
United States of America
77843-4253
+1 9794581498
rbkreider@tamu.edu

Type(s)
Public

Contact name
Mr Christopher Rasmussen

ORCID ID
https://orcid.org/0009-0005-8941-3067

Contact details
675 John Kimbrough Blvd.
Suite #206
College Station
United States of America
77843-4253
+1 9794581741
crasmussen@tamu.edu

Additional identifiers

Study information

Scientific Title
Effects of six weeks of guanidinoacetic acid supplementation with and without creatine monohydrate on cognitive function and markers of health in healthy adults

Acronym
GAA/CrM Study

Study objectives
The main objectives of this study are to evaluate the effects of short-term Guanidinoacetic Acid (GAA) supplementation with and without Creatine Monohydrate (CrM) on markers of cognitive function and health.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 10/01/2025, 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: STUDY2024-1370

Primary study design
Interventional

Study design
Randomized double-blind placebo-controlled clinical trial

Study type(s)
Treatment

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

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

Treatment 1. Placebo (2 x 1 g maltodextrin + 5 g maltodextrin)
Treatment 2. GAA (2 x 1 g GAA + 5 g maltodextrin)
Treatment 3. GAA + CrM (2 x 1 g GAA + 5 g CrM).

The supplements will be prepared in powder form in generic, labeled capsules from the sponsor. Participants will be asked to consume two doses of their assigned supplement per day (one with breakfast and one with dinner) for six weeks.

Intervention Type
Supplement

Primary outcome(s)
1. A range of cognitive skills including processing speed, memory, attention, executive function, and visuoperceptual skills measured using the COMPASS Cognitive Function Test Battery at 0,6 weeks.

Key secondary outcome(s)
1. Body weight measured using a calibrated, digital scale at 0,6 weeks.
2. Resting hemodynamics (Heart Rate and Blood Pressure) measured using a sphygmomanometer at 0,6 weeks.
3. Body composition (%) measured using a calibrated DXA at 0,6 weeks.
4. Complete Blood Count (CBC) measured using automated analyzers from Clinical Pathology Laboratories (CPL) at 0,6 weeks.
5. Blood Chemistry Panel (Chem Panel) measured using automated analyzers from Clinical Pathology Laboratories (CPL) at 0,6 weeks.
6. Blood Lipids (Lipid Panel) measured using automated analyzers from Clinical Pathology Laboratories (CPL) at 0,6 weeks.
4. Homocysteine (Hcy) measured using automated analyzers from Clinical Pathology laboratories (CPL) at 0,6 weeks.
5. Menstrual experiences for females using the Menstrual Status Questionnaire at 0,6 weeks.
6. Menopause experiences for females using the Menopause Status Questionnaire at 0,6 weeks.
7. Adverse effects assessed using Side-Effects Assessment at 0,6 weeks.

Completion date
20/09/2025

Eligibility

Key inclusion criteria
1. Male or female between the ages of 18 and 65 years.
2. Participant has the ability to complete the study, comply with the study procedures, consume the investigational product daily for the duration of the study and provide voluntary written informed consent to participate in the study.
3. Participant is willing to refrain from alcohol intake and ingesting caffeinated foods and beverages for 48-hours prior to each testing session.
4. Participant is willing to not consume dietary supplements that may affect cognitive function during the study.
5. Participant is willing to comply and understand the cognitive function tests.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
61

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 the results of the study.
8. Participant has a known allergy to meat or fish, GAA, CrM, or maltodextrin.

Date of first enrolment
10/02/2025

Date of final enrolment

20/09/2025

Locations

Countries of recruitment
United States of America

Study participating centre
Exercise & Sport Nutrition Laboratory
675 John Kimbrough Blvd.
Suite #206
College Station
United States of America
77843-4253

Sponsor information

Organisation
The WoodNext Foundation

Funder(s)

Funder type
Charity

Funder Name
The WoodNext Foundation

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study will be available upon request from Dr. Richard Kreider at rbkreider@tamu.edu.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		12/09/2026	14/09/2026	Yes	No