

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

|  |   |   |
|--|---|---|
| <b>Submission date</b><br>10/11/2025   | <b>Recruitment status</b><br>No longer recruiting | <input type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol                                  |
| <b>Registration date</b><br>12/11/2025 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input type="checkbox"/> Results                                  |
| <b>Last Edited</b><br>11/11/2025       | <b>Condition category</b><br>Other                | <input type="checkbox"/> Individual participant data<br><input checked="" type="checkbox"/> 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. 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 goal 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 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**

### **Clinical Trials Information System (CTIS)**

Nil known

### **Protocol serial number**

Nil known

## **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

## **Study design**

Randomized double-blind placebo-controlled clinical trial

## **Primary study design**

Interventional

## **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**

Adult

**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](mailto:rbkreider@tamu.edu).

**IPD sharing plan summary**

Available on request