The Ergogenic Effects of Glutamine: Counterpoint

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Hypothesis

Our Approach: Glutamine supplementation does not influence anti-catabolic activity and glycogen synthesis so as to improve responses to resistance training.

Opposition: Glutamine supplementation does influence anti-catabolic activity and glycogen synthesis so as to improve responses to resistance training.
Our *counterpoint* argument is focused on...

- Glutamine is not involved in the muscle repair process
- Glutamine supplementation does not change lean tissue mass.
- Glutamine supplementation does not significantly increase intramuscular glycogen levels

Critique the opposing *point* argument
Non Clinical Uses

- Glutamine supplements can be used for rehydration, which will increase time to fatigue during exhaustive exercise \( (Hoffman\ et\ al,\ 2010) \)

Clinical Uses

Oral glutamine supplementation is used to:

- Minimize side effects of chemoradiotherapy including weight loss and esophagitis \( (Gul\ et\ al,\ 2010) \)
- Compensate for ischemia-reperfusion injuries when renal arginine is reduced by producing citrulline and arginine \( (Brinkmann\ et\ al,\ 2016) \)
Proposed Mechanism

Glutamine (Gln) is *glycogenic* – can be converted to glucose by *gluconeogenesis* to fuel metabolic reactions:

- Gln is converted to glutamate by gln synthase. Transamination reaction with pyruvate produces alanine (also glycogenic).
- Glucose production initiates insulin release, activates glycogen synthase. Increases hepatic glycogen stores, reduces catabolic amino acid release.

Fig. 1: Net change in glycogen storage in μmol g⁻¹·wet wt following Saline, Alanine (Ala) + Glycine (Gly), and Glutamine infusions. * = Significant differences at 5% by repeated measures ANOVA. *(Varnier et al, 1995)*
Proposed Mechanism

Exogenous glutamine supplements *allegedly* maintain muscle mass by fuelling gluconeogenesis in place of stored glutamine.

Fig. 2: Increases plasma [glutamine] and [insulin] in \( \mu \text{mol} \cdot \text{l}^{-1} \) during glutamine (■) infusion. * = significant difference 5% repeated measures ANOVA vs. pre-infusion concentrations.

*(Varnier et al, 1995)*
Proposed Mechanism

Ingestion of glutamine can initiate growth hormone (GH) release, therefore has an anabolic effect.

- Glutamine converts to citrulline in the small intestine, which supports renal arginine synthesis.
- Heightened plasma arginine stimulates the release of GH.

Supplements increase glutamine delivery to small intestine and increase downstream GH release. (Welbourne, 1995)

Fig. 3: [GH] in mol/L before and after supplement. * = Significant at 5% by repeat measures ANOVA. Average for all subjects (●).
Recommended Daily Allowance (RDA)

Conflicting data on glutamine supplementation exists therefore a Dietary Reference Intake cannot be DRI-ved

(Rathmacher et al, 2004) performed a double blind study which concluded an observed safe limit of **14g/day**

(Candow et al, 2001) reported supplementing as high as **45g/day** without subjects reporting negative effects
Safe use

**Observed toxicity:** plasma glutamine = 1.3 mmol/L

**Case Study:** A woman overdosed on acetaminophen, causing high plasma glutamine.

**This Resulted in:** Osmotic stress and Cerebral edema

Short term effects:
- Confusion
- Agitation

![Fig. 4: Recorded plasma [glutamine] against hrs after acetaminophen ingestion. Toxic levels at 120 hrs.](Brusilow et al, 2011)
Research Outcome #1 Refuting Ergogenic Effects

**Methods:** (n=89) Rats on 2 week weight training program.

Rats received:
1. High dose of Sustamine™ (alanine + glutamine supplement)
2. Low dose of Sustamine™
3. Whey Protein supplement
4. Placebo supplement (control)
5. Sedentary without supplement (control)

Post exercise muscle samples were taken to evaluate the activation of the m-TOR muscle regeneration pathway and associated proteins such as p70S6K.

*(Wang et al, 2015)*
#1 Continued

**Results:** Flexor hallucis longus muscle (FHL) samples showed little phosphorylation of P70S6K in both Sustamine groups, therefore there was less activation of protein synthesis.

Supplementation of glutamine induced less protein synthesis, therefore had a poor anabolic response.

*Fig. 5: Modified from Wang et al, 2015*

Fig. 5: Amount of P70S6K activation as a % of standard levels across experimental conditions. * = significant at $P < 0.05$ vs Whey. Low sustamine (LSUS) and high sustamine (HSUS) groups show significantly less activation than whey condition.
Research Outcome #2 Refuting Ergogenic Effects

**Methods:** (n=31) Previously active subjects participated in a 6 week resistance training program with various supplementations. Double blind, repeated measures.

Subjects were supplemented:
1. Glutamine
2. Placebo

Because glutamine is typically consumed through oral supplementation, this study best represents the population.

DXA imaging was used pre and post program to quantify changes to lean tissue mass.

*(Candow et al, 2001)*
#2 Continued

**Results:** Both glutamine and placebo groups increased lean tissue mass to the same degree between weeks 1-6.

Equal slope between groups shows improvement to the same extent. Therefore glutamine supplementation provided no anabolic advantage to resistance training. *(Candow et al, 2001)*

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**Fig. 6:** Mean lean tissue mass (kg) for glutamine (■) and placebo (▲) groups between weeks 0-6. Error bars show SEM while * = significance at $P < 0.05$ compared to week 0.
Research Outcome #3 Refuting Ergogenic Effects

**Methods:** (n=8) Trained subjects performed glycogen depleting exercise with supplement ingestion 15 minutes following completion. Repeated measures study.

Subjects received:
1. Glucose (control)
2. Glucose + glutamine
3. Glucose + wheat protein (hi glutamine dose)
4. Glucose + whey protein (normal glutamine dose)

A muscle biopsy was taken before and after supplementation to measure muscle glycogen resynthesis.

*(Van Hall et al, 2000)*
#3 Continued

**Results:** No significant difference in rate of glycogen resynthesis between control and glutamine conditions.

Even after glycogen depleting exercise, there was no restorative benefit to glutamine supplementation.

Fig. 7: Rate of muscle glycogen resynthesis in mmol/ (kg dry muscle.hour) during recovery from intense exercise after glucose, or glucose + glutamine (Gln), wheat protein, or whey protein supplementation. Values are means +/- SEM.  

*(Van Hall et al, 2000)*
Evidence to Refute Effect #1

Methods: (n=18) Subjects performed glycogen depleting exercise for 90 minutes with intermittent sprint periods, followed by supplement infusion 30 minutes after completion of exercise.

Subjects received:
1. Glutamine infusion
2. Alanine + Glycine infusion
3. Control: saline infusion

Muscle tissue samples were collected before and after infusion to measure muscle glycogen stores.

(Varnier et al, 1995)
#1 Continued

**Results:** Glutamine infusion group had 2-fold increase in overall Glycogen (Gly) storage after infusion. Supports that glutamine infusion promoted skeletal muscle glycogen storage.

**Refute:** Glycogen depleting training causes greater stress, and muscle glycogen depletion than resistance training. Physiological response is different. Similar studies also show converse results *(see G. van Hall et al.)*

![Fig. 8: Net Glycogen accumulation μmol g⁻¹·wet wt during three infusions. * = significant differences at 5% by repeat measures ANOVA](Varnier et al, 1995)
Evidence to Refute Effect #2

**Methods:** (n=9) Subjects ingested supplement.

Subjects received:
- Control: Vehicle- Carbonated soft drink (pH 3.8, 20g glucose)
- Vehicle + 2g L-glutamine

Blood samples taken prior, then 30, 60 and 90 minutes after supplementation. Samples were measured for plasma glutamine, and growth hormone (pGH).

*(Welbourne, 1995)*
Results: Recorded 4-fold increase in plasma growth hormone (90 min) following increase in plasma glutamine, promotes protein synthesis.

Refute: 1 hr of moderate exercise causes 20-fold increase in plasma growth hormone, 4-fold increase is minor in comparison (Candow et. al)

Fig. 9: Plasma growth hormone concentrations (mol/L) before and after supplement was given. Average for all subjects (●)  
(Welbourne, 1995)
In Conclusion…

Glutamine supplementation *does not* influence anti-catabolic activity and glycogen synthesis so as to improve responses to resistance training.
References


