1. Introduction

• Acute tryptophan depletion (ATD) has commonly been used to examine the behavioral and cognitive consequences of depleting the serotonergic system.

• The specificity of ATD to modulate serotonergic activity alone has recently come under scrutiny (1) and the impact of ATD on kynurenine production, the predominant pathway of kynurenine metabolism (Figure 1), has yet to be determined.

• Manipulating kynurenine and downstream metabolites may modulate central nervous system glutamatergic and cholinergic signaling, key neurotransmitter systems in regulating cognitive function, in addition to affecting gastrointestinal symptoms (Figure 3).

2. Aims

• To determine if experimentally modulating tryptophan availability using acute tryptophan depletion (ATD) alters peripheral kynurenine production in patients with IBS.

• To investigate if modulating peripheral kynurenine production affects central measures of cognition, mood and arousal, in addition to gastrointestinal symptoms.

3. Methods

Study Design:
- Double blind, placebo controlled, crossover design.

Study Population:
- 9 female, Rome III positive IBS patients & 15 matched female healthy control participants (see Table 1 for sample characteristics at baseline).

- All participants screened for psychiatric co-morbidity using the MINI Psychiatric interview.

- Females not using contraceptive tested during follicular phase of cycle.

4. Results

ATD Modulates Plasma Kynurenine

Table 1: Comparison between IBS patients and healthy controls on demographic and clinical characteristics. Data are shown as mean ± standard deviation (SD) and percentages where appropriate. *p < 0.05 compared to control group using ANOVA (ATD), t-test (IBS vs. control), or Mann-Whitney U test (IBS vs. control) with Bonferroni correction for multiple testing. **p < 0.05 compared to control group using ANOVA (ATD), t-test (IBS vs. control), or Mann-Whitney U test (IBS vs. control) with Bonferroni correction for multiple testing.

ATD Improves Visuospatial Memory in IBS

5. Conclusions

- Our results further question the specificity of ATD as an exclusively serotonergic challenge and suggest that via kynurenine production, this protocol may impact on cognition.

- The impact of ATD on glutamatergic and cholinergic neurotransmitter systems may lead to visuospatial memory impairments. However, this effect only emerged in our vulnerable IBS cohort who have pre-existing alterations in both kynurenine production and cognitive performance.

- These data have important implications for the current conceptual basis and specificity of the ATD protocol. Moreover, they provide some much needed insight to the central mechanisms underlying the cognitive neurobiology of IBS.