Dietary Amino Acids and Proteins Influence Serotonin Synthesis in Brain Neurons

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Neuronal Serotonin Synthesis & Metabolism
Source of Neuronal Tryptophan
**PLASMA**

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Plasma TRP (nmol/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>50</td>
</tr>
<tr>
<td>1</td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td>100</td>
</tr>
</tbody>
</table>

- Fasting
- Carbs
- Protein

**BRAIN**

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Brain TRP (nmol/gram)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
</tr>
</tbody>
</table>

- Carbs
- Fasting
- Protein
Source of Neuronal Tryptophan

* Serum TRP/ΣLNAA
• Serotonin synthesis in brain neurons is influenced by normal changes in brain TRP levels

• Brain TRP levels are influenced by changes in blood levels of TRP and the other LNAA: BBB competition is important!

• Carbohydrates raise brain TRP (and 5HT) while protein does not: competition explains dichotomy.
The bovine protein α-lactalbumin increases the plasma ratio of tryptophan to the other large neutral amino acids, and in vulnerable subjects raises brain serotonin activity, reduces cortisol concentration, and improves mood under stress\textsuperscript{1-3}.

\textit{C Rob Markus, Berend Olivier, Geert EM Panhuysen, Jan Van der Gugten, Martine S Alles, Adriaan Tuiten, Herman GM Westenberg, Durk Fekkes, Hans F Koppeschaar, and Edward EHF de Haan}

\textit{Am J Clin Nutr 2000; 71: 1536-1544.}
Source: Feurte S et al., *Nutr Neurosci* 4: 413-418, 2001
Extracellular 5HT levels from hypothalamus in rats ingesting either casein (*white bars*) or lactalbumin (*black bars*) diets.

*P<0.05 or ***P<0.001 vs day 0; ++P<0.01 vs casein diet.

In Vivo Microdialysis in Rat Brain
Meal ingestion, amino acids and brain neurotransmitters: Effects of dietary protein source on serotonin and catecholamine synthesis rates

SuJean Choi, Briana DiSilvio, Madelyn H. Fernstrom, John D. Fernstrom

*Physiology & Behavior* **98**: 156-162, 2009

1. Give rats a meal containing 17% protein at dark onset.
2. Meal contains no protein (*carbs + 5% fat only*) or the same formulation with one of 5 proteins (*Lactalbumin, Casein, Gluten, Soy Protein, Zein*).
3. Two hr after meal presentation, inject a drug to allow 5HT synthesis to be measured.
4. Sacrifice rats 30 minutes later.
Effects of Single Meals Containing Different Proteins: Rat Study

Source: Choi S et al., Physiol Behav 98: 156-162, 2009
Effects of Single Meals Containing Different Proteins: Rat Study

![Graph showing effects of different meals on serum TRP ratio and cortex TRP levels.](graph.png)

Source: Choi S et al., *Physiol Behav* 98: 156-162, 2009
Effects of Single Meals Containing Different Proteins: Rat Study

Source: Choi S et al., Physiol Behav 98: 156-162, 2009
Effects of Chronic Diets Containing Different Proteins: Rat Study

Effects of Chronic Diets Containing Different Proteins: Rat Study

Dietary Protein Ingestion has the same plasma effects in humans & rats

Choi S et al., *Physiol Behav* 28: 156-162, 2009
Fernstrom JD et al., *Clin Nutr* 32: 1073-1076, 2013
Speculation


Serotonin and depression: pathophysiological mechanism or marketing myth?

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Acute Tryptophan Depletion: Depression

- Depressed Px (n=18) in remission on meds.
- ATD ± TRP @ 9AM.
- HDRS @ 1, 2, 3, 4, 6, 8 Hr.
- Balanced, cross-over design.
- 2-7 days between tests.

Acute Tryptophan Depletion: Biochemistry

- Healthy subjects (n=6) admitted to CRC.
- Low monoamine & low TRP diet from day 1.
- Lumbar catheter placed on day 8.
- ATD drink ingested on day 9 and samples drawn.