



Management of Monoamine Related Relative Nutritional Deficiency

Two primary categories of nutritional deficiency exist. An absolute nutritional deficiency occurs when nutrient intake is not sufficient to meet the normal needs of the system. A relative nutritional deficiency exists when nutrient intake and systemic nutrient levels are normal while a change occurs in the system that induces a nutrient intake requirement that cannot be supplied from diet alone.

Int J Gen Med. 2012; 5:135-42. Epub, 2012 February 14.

Reuptake inhibitors may facilitate conditions that deplete monoamines. Reuptake inhibitors will not function if monoamine depletion is significant. When significant monoamine depletion occurs, the placebo effect and/or drug effect may no longer be observed.

Drug Healthc Patient Saf. 2011; 3:69-77. Epub, 2011 October 20.

THE MONOAMINE NEUROTRANSMITTERS (Serotonin, dopamine, norepinephrine, epinephrine)

THE PROBLEM: Inadequate levels of neurotransmitters

PERSPECTIVE

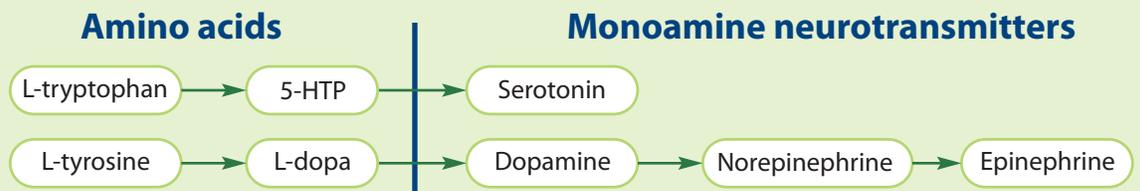
- Drugs do not increase the total number of neurotransmitters in the brain.
- Dietary administration of CHK Nutrition's amino acid formulas are designed to support appropriate dopamine and serotonin levels within the body.
- Reuptake inhibitors release monoamine neurotransmitters, but do not facilitate synthesis.
- When initial levels are not adequate or depletion destroys enough molecules, a relative nutritional deficiency occurs which can not be corrected with dietary modification alone (see page 2).
- In order to address the relative nutritional deficiency, properly balanced supplemental nutrients must be administered at levels beyond what can be obtained from diet alone.
- When no relative nutritional deficiency exists, there are adequate neurotransmitter levels in the system to facilitate reuptake inhibitor function.
- When no relative nutritional deficiency exists, optimal neurotransmitter function facilitates adequate post-synaptic flow of electricity and regulatory function resulting in optimal health and wellness.

There are two basic types of nutritional deficiencies:

- Inadequate nutrient intake
- "Relative nutritional deficiency" occurs when changes in the system status induce nutritional needs beyond the abilities of dietary modification.

When reuptake inhibitors stop working, the primary cause is a therapeutically induced "relative nutritional deficiency."

Drug Healthc Patient Saf. 2011; 3:69-77. Epub, 2011 October 20.



CHK Nutrition's products have been formulated to properly address monoamine related relative nutritional deficiency.

Reuptake inhibitor induced relative nutritional deficiency

Illustrations courtesy of the National Institute of Drug Abuse

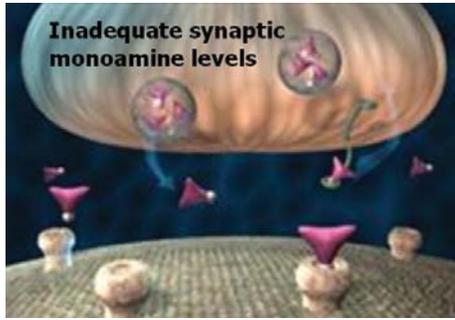


Figure 1: Inadequate levels of neurotransmitters in the synapse are associated with compromised electrical flow in the post-synaptic neurons leading to suboptimal regulation of function and/or development of symptoms.

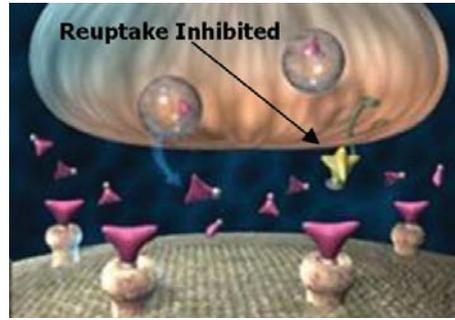


Figure 2: The administration of reuptake inhibitors block monoamine transport back into the pre-synaptic neuron leading to a net redistribution of neurotransmitter molecules from the pre-synaptic neuron into the synapse. Increased levels of synaptic monoamines result in increased post-synaptic electrical flow.

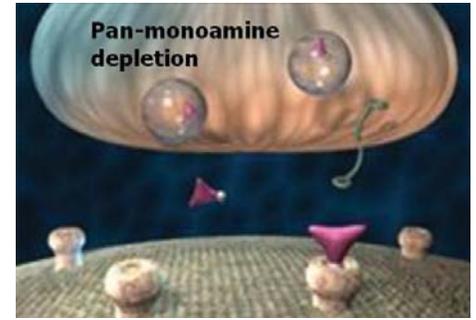


Figure 3: When monoamines are in the pre-synaptic vesicles, they are not exposed to the enzymes that catalyze metabolism (MAO and COMT). When monoamines are relocated outside of the pre-synaptic vesicles into the synapse, they are exposed at a greater frequency to these destructive enzymes. Reuptake inhibitors force monoamines to remain in the synapse resulting in increased monoamine metabolic enzymatic activity. Relative nutritional deficiency occurs when monoamine enzymatic activity destroys enough monoamines that the system needs higher than normal monoamine levels in order to function properly.

SSRIs at therapeutic doses block this reuptake of serotonin by platelets leading to a depletion of serotonin after several weeks of treatment.

Am J Med. 2006 September; 119(9):719-27.

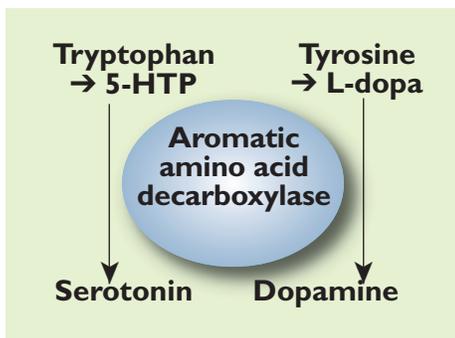
Improperly balanced amino acid precursors deplete centrally acting monoamine neurotransmitters

Monoamine neurotransmitters and their amino acid precursors exist in two distinctly different physiological states:

- **THE ENDOGENOUS STATE** found when no amino acid precursors are being administered.
- **THE COMPETITIVE INHIBITION STATE** found when significant amounts of serotonin and dopamine amino acid precursors are being administered simultaneously.

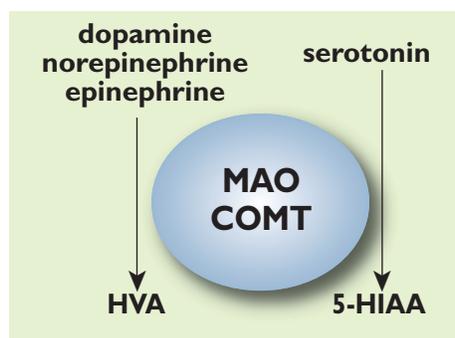
Br J Pharmacol. 1996 March; 117(6):1187-92.

How improperly balanced amino acids deplete monoamine neurotransmitters



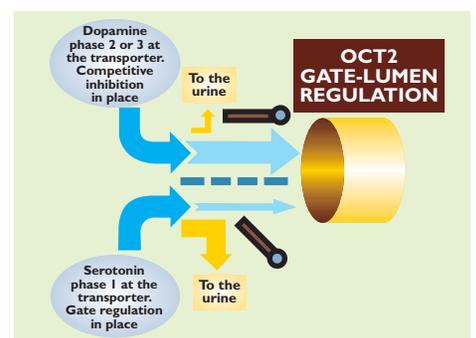
SYNTHESIS IN COMPETITIVE INHIBITION:

The same enzyme, L-aromatic amino acid decarboxylase (AAAD), is responsible for the synthesis of serotonin and dopamine. In the competitive inhibition state, if amino acid precursors of one system dominate the AAAD, an environment is created which decreases the synthesis of the non-dominant system resulting in its depletion.



METABOLISM IN COMPETITIVE INHIBITION:

Serotonin and Dopamine are both metabolized by the monoamine oxidase (MAO) enzyme. Significantly higher levels of one system increases MAO activity which leads to increased metabolism and depletion of the non-dominant system.



TRANSPORT IN COMPETITIVE INHIBITION:

Serotonin, dopamine, and their amino acid precursors compete for transport by the organic cation transporters. Significant increases in one will decrease monoamine and precursor transport of the non-dominant system. Transport of precursors into the cells is required for synthesis to take place.

THE PROTOCOL

For the nutritional management of monoamine neurotransmitter relative nutritional deficiencies. When a patient presents with monoamine neurotransmitter depletion, CHK Nutrition's products are designed to provide the proper balance of nutrients which may provide management of monoamine related relative nutritional deficiencies.



NeuroReplete

Take four NeuroReplete pills in the morning and four NeuroReplete pills approximately 5 to 6 hours before bedtime (usually around 4 PM for most individuals).

CysReplete

Take two pills of CysReplete, three times a day with the first dose at noon.

CysReplete is required since ingestion of L-tyrosine and/or L-dopa is associated with depletion of sulfur amino acids.



SIDE EFFECT MANAGEMENT

GI UPSET → ON START UP

THE PROBLEM: Approximately 1 to 2% of patients experience GI upset or nausea when starting amino acids. Typically this starts with the first dose and builds with every dose until the third day, at which point the patient can no longer tolerate the symptoms.

THE CAUSE: Patients who have the greatest neurotransmitter depletion often experience GI upset or nausea when starting the amino acids. These patients may benefit the most from amino acid supplementation to address their relative nutritional deficiency.

MANAGEMENT: Restart NeuroReplete taking only one pill at bedtime. It is important that the pill is taken when the patient is ready to sleep, not when getting in to bed to watch television or read a book. If the patient is able to fall asleep within 20 minutes of taking the NeuroReplete pill, there should be no problems with GI upset. After 3 or 4 nights without GI upset, increase to two pills of NeuroReplete at bedtime. Once the patient is able to take two pills at bedtime without GI upset, start one NeuroReplete pill in the morning. After 3 to 4 days without problems, increase the patient to two NeuroReplete pills. Once the patient is taking two NeuroReplete in the morning and two NeuroReplete at night, it is recommended that the health care provider obtain a urinary transporter evaluation.

SIDE EFFECTS

THE PROBLEM: The recommendation is to leave all drugs in place when starting the amino acids. In 3 to 5% of patients, side effects not associated with the amino acids may occur when starting or changing the amino acid dose.

THE CAUSE: In patients taking a reuptake inhibitor, as amino acids are administered, drug side effects may display as well.

WHEN MANAGED PROPERLY, SIDE EFFECTS CAN BE EFFECTIVELY ADDRESSED. THESE AMINO ACID FORMULATIONS DO NOT NEED TO BE STOPPED ON A LONG-TERM BASIS.

ADDRESSING THE RELATIVE NUTRITIONAL DEFICIENCY

APPLICATIONS

When addressing relative nutritional deficiency:

- It takes 3 to 5 days to achieve amino acid equilibrium and observe the full effects

ADMINISTERING ONLY:

- L-tryptophan may deplete dopamine
- 5-HTP may deplete dopamine
- L-tyrosine may deplete serotonin
- L-dopa may deplete serotonin

Serotonin and dopamine amino acid precursors need to be administered in proper balance.

(See the bottom of page 2 for the mechanism.)

Possible Amino Acid Only Side Effect Profile

Dry mouth	34 (2.1%)
Insomnia	14 (0.9%)
Headache	12 (0.7%)
Nausea	10 (0.6%)
Dizziness	6 (0.4%)
Constipation	6 (0.4%)

All other side effects occur at a rate less than 1 in 500 visits

Kohlstadt I. editor. Food and Nutrients in Disease Management CRC Press; 2009, 465-481

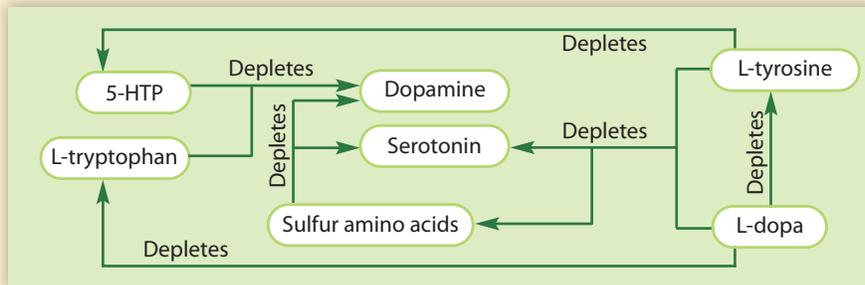


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Other causes of neurotransmitter depletion

Administration of improperly balanced monoamine amino acid precursors and sulfur amino acids may deplete neurotransmitters



CHK Nutrition provides the amino acids and technology to properly manage depletion induced by amino acids and other substances.

"At 200 μ m 5-HTP, **dopamine synthesis** from both tyrosine and DOPA was **inhibited** about 70%." *Journal of Neurochemistry*. Vol. 30. pp. 465-470. Elsevier Publishing, 1978 March 4.

"A possible mechanism for the **depletion of dopamine** by 5-HTP might be attributable to displacement of the dopamine stores by the serotonin formed from 5-HTP." *Arch Pharmacol*, 303 pp. 63-72. Elsevier Publishing, 1978 February.

"Other studies show that S-adenosyl-methionine **depletes dopamine.**" *Life Sciences* Volume 61, Issue 5, Pages 495-502. Elsevier Publishing, 27 June 1997.

"Elevations in brain tyrosine appear to contribute to the long term **serotonin depletions** in the striatum and hippocampus." *Journal of Neuroscience*, 26(1):290-299 Society for Neuroscience. 2006 January, 4.

"L-dopa-induced **depletion of serotonin.**" *Life Sciences* Vol. 20, pp. 1675-1680. Elsevier Publishing, 1977 May 15.

"**Serotonin** content was significantly **decreased** in all brain regions studied 30 min after long-term L-DOPA." *Cell Mol Neurobiol* 27:985-996. Springer Publishing, 2007 October 13.

"L-dopa has been shown to **deplete** the concentration of **S-adenosyl-methionine.**" *Pharmacology Biochemistry and Behavior* Volume 43, Issue 2, Pages 423-431. Elsevier Publishing, 1992 October.

"Intraperitoneal injections of L-dopa (100 and 200 mg/kg) **decreased** the concentrations of **tryptophan, tyrosine and serotonin.**" *European Journal of Pharmacology* 14 (1971) 393-396. Elsevier Publishing, 1971 May.

CysReplete

Supplement Facts

Serving Size 2 Capsules
Servings per Container 90

	Amount Per Serving	%DV*
Selenium (as Selenium amino acid Chelate)	134 mcg	192%
Folate	133 mcg	33%
L-Cysteine HCl	1500 mg	†

Does not contain wheat, corn, soy, sucrose, salt, starch, yeast, artificial flavors, artificial colorings, or other known allergens.

* Percent Daily Values (DV%) are based on a 2,000 calorie diet.

† Daily Value (DV) not established

Other Ingredients: Gelatin, Magnesium Stearate, Rice Flour

NeuroReplete

Supplement Facts

Serving Size 4 Capsules
Servings per Container 60

	Amount Per Serving	%DV*
Vitamin C (Ascorbic Acid)	500 mg	833%
Calcium (from Calcium Citrate)	110 mg	11%
Vitamin B6 (Pyridoxine hydrochloride)	37.5 mg	1875%
Folate	200 mcg	50%

Proprietary blend of L-Lysine, 5-Hydroxytryptophan, L-Tyrosine	1,900 mg	†
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Does not contain wheat, corn, soy, sucrose, salt, starch, yeast, artificial flavors, artificial colorings, or other known allergens.

* Percent Daily Values (DV%) are based on a 2,000 calorie diet.

† Daily Value (DV) not established

Other Ingredients: Vegetable-based capsules, Rice Flour, Silicon Dioxide, Cellulose and Magnesium Stearate