DBS LABS

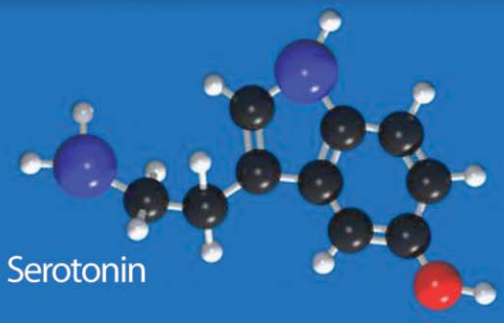
MTO Instructions

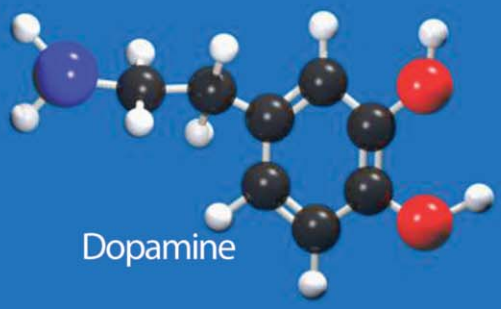
The peer-reviewed science of MTO with testing and management guidelines

Get the information you need to make decisions when serotonin and/or dopamine concentrations are low or inadequate.

Monoamine Transporter Optimization™

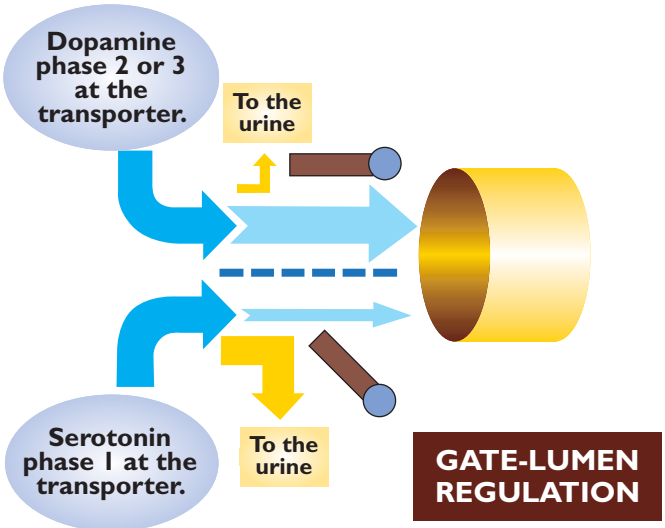
One of the most profound and far-reaching advances in laboratory medicine, EVER!™





Dual gate lumen transporters

are the primary determinant of serotonin and dopamine concentrations in the brain



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PERSPECTIVE

When symptoms relate to low or inadequate serotonin, dopamine, norepinephrine, and epinephrine levels, a relative nutritional deficiency exists.

ACRONYMS AND DEFINITIONS:
RND: Relative Nutritional Deficiency
Symptoms: Symptoms relating to RND
OCT: Organic Cation Transporter
MTO: Monoamine Transporter Optimization

THE PROBLEM: Inadequate (low or not high enough) serotonin and/or catecholamines (dopamine, norepinephrine, epinephrine)

DRUGS

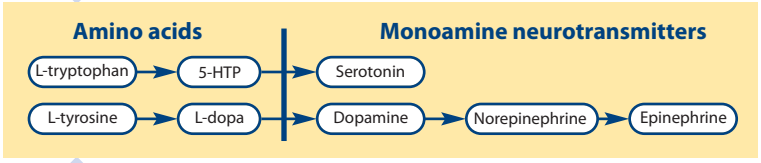
Reuptake inhibitor drugs do nothing to increase the total number of these neurotransmitter molecules in the brain.

Reuptake inhibitors work by moving neurotransmitters from one place to another, they do not increase the total number of neurotransmitter molecules in the brain.

NUTRIENTS

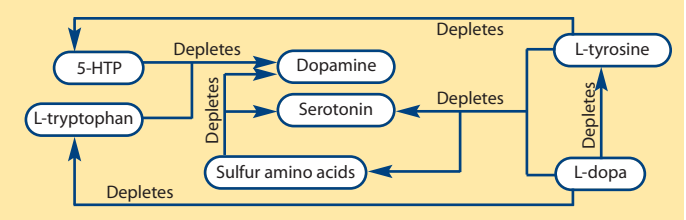
Serotonin, dopamine, norepinephrine, and epinephrine do not cross the blood-brain barrier. They cannot be replenished from peripheral stores.

The natural way to increase the total number of monoamine neurotransmitter molecules in the brain is through simultaneous administration of properly balanced serotonin and dopamine amino acid precursors.



5-HTP and L-dopa are synthesized freely into serotonin and dopamine, respectively, without biofeedback inhibition. This enables serotonin and dopamine levels to be raised as high as needed without restriction. Resolution of relative nutritional deficiency (RND) is not dependent upon attaining serotonin and dopamine levels that are high enough. Achieving proper balance between serotonin and dopamine in transport will properly address the RND.

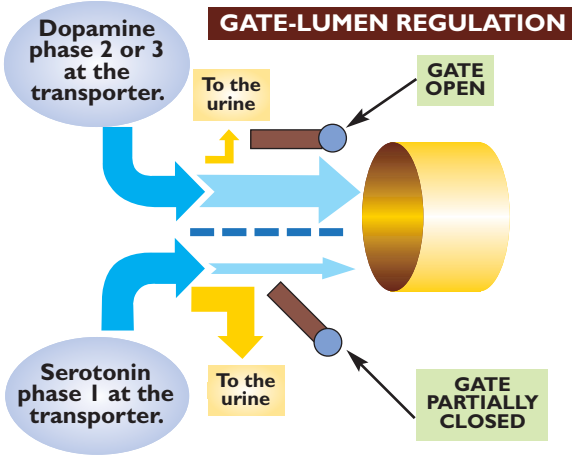
When neurotransmitter levels are not adequate, (low or not high enough) while on an optimal normal diet, a "relative nutritional deficiency" exists. Improperly balanced administration of serotonin and/or dopamine amino acid precursors may lead to an amino acid relative nutritional deficiency.



Administration of amino acids needs to be in proper balance.

Monoamine Transporter Optimization (MTO)

Transporters move neurotransmitters and their amino acid precursors in and out of cellular structures. Transporters are the primary determinant of neurotransmitter concentrations. MTO facilitates the determination and establishment of the optimal flow of these neurotransmitters through the transporters.



	GATE	LUMEN
PHASE 1	Partially closed	Unsaturated
PHASE 2	Open	Unsaturated
PHASE 3	Open	Saturated

The "dual gate lumen" transporter model is the foundation of MTO. Ascertaining the phase (1, 2, or 3) is a determination of the status of the serotonin or dopamine entrance gates and the transporter lumen saturation status.

Transporters determine the synaptic concentrations of serotonin, dopamine, and norepinephrine.

Whenever synaptic serotonin, dopamine and/or norepinephrine are low or inadequate while on a normal diet, a "relative nutritional deficiency" (RND) exists.

This technolology is indicated whenever the care giver determines a condition exists where serotonin and/or dopamine levels are not adequate.

FIGURE 1

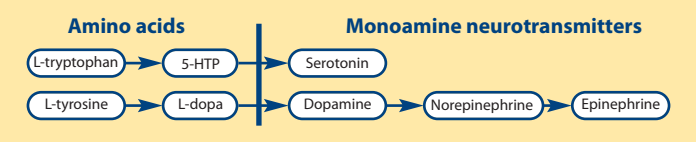
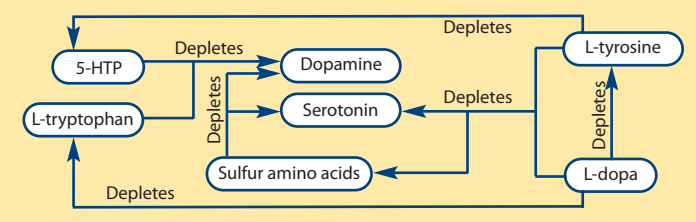


FIGURE 2: Solve this puzzle and you master serotonin, catecholamine, and sulfur amino interaction



AMINO ACID PRECURSORS AND NEUROTRANSMITTERS EXIST IN TWO DISTINCTLY SEPARATE STATES

"THE ENDOGENOUS STATE" is the normal day-to-day state that exists when taking no supplemental amino acids.

"THE COMPETITIVE INHIBITION STATE" is found when the patient is simultaneously taking serotonin and dopamine amino acid precursors in significant amounts.

NUTRITIONAL DEFICIENCIES

Two types of nutritional deficiency exist:

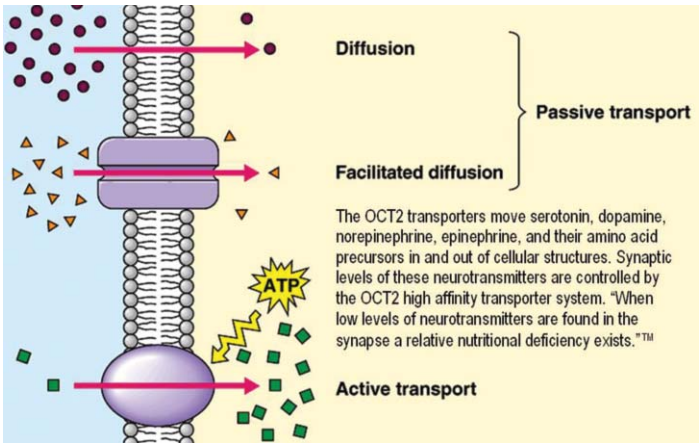
ABSOLUTE NUTRITIONAL DEFICIENCY occurs when there are not enough nutrients in the diet.

RELATIVE NUTRITIONAL DEFICIENCY (RND) occurs when systemic needs have increased to a point where optimal dietary modification is no longer possible.

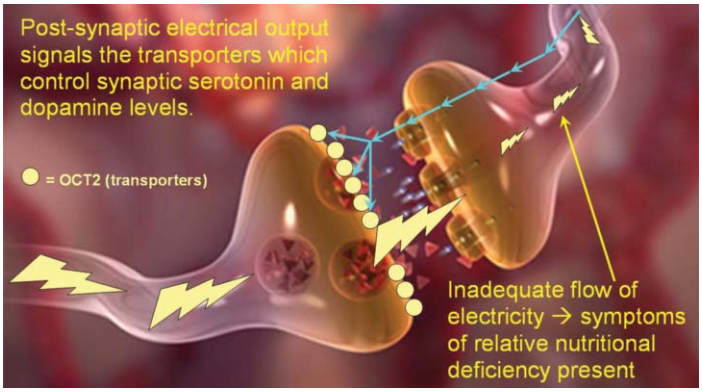
Administration of improperly balanced amino acid precursors of one neurotransmitter may deplete other amino acid precursors and their neurotransmitters leading to an "amino acid-induced RND" (relative nutritional deficiency).

LOW OR INADEQUATE LEVELS OF SEROTONIN AND/OR DOPMAINE = RELATIVE NUTRITIONAL DEFICIENCY

- Serotonin and dopamine do not cross the blood-brain barrier.
- One way to increase the total number of serotonin and/or dopamine molecules in the brain is through administration of amino acid precursors (Figure 2) which cross the blood-brain barrier and are then synthesized into new serotonin and/or dopamine molecules.
- When the patient is on a normal diet and central nervous system levels of neurotransmitters are not adequate MTO defines the optimal serotonin and dopamine correction points to compensate for the monoamine related relative nutritional deficiency.



Types of transport are passive and active. Cell walls are lipophilic. Hydrophilic substance such as serotonin and dopamine along with their amino acid precursors do not cross the cell wall, they are transported via the Organic Cation Transporters (OCT).



The reuptake transporters (OCT2) are the primary determinant of synaptic serotonin and dopamine levels
The leading cause of chronic electrical dysfunctional in the system (pre-synaptic neuron, synapse, post-synaptic neuron) is permanent damage to the post-synaptic neurons. The electrical output of the post-synaptic neurons induces a signaling of the pre-synaptic serotonin and dopamine reuptake transporters encoding them with the configuration that optimizes the movement of electricity across the synapse.

When there low or inadequate serotonin, dopamine, norepinephrine, and epinephrine levels are found, a relative nutritional deficiency exists.

TESTING PROTOCOL

INITIAL VISIT: Orientation (See page 8)

Peer-reviewed literature notes, "Baseline testing prior to starting amino acids is of no value."

START AMINO ACIDS: See the next page for recommended starting amino acid dosing required before testing.

FOLLOW-UP VISIT IN ONE WEEK (see below)

RND SYMPTOMS UNDER CONTROL: Continue the starting dose of amino acids then schedule a follow-up visit in 1 week.

RND SYMPTOMS NOT UNDER CONTROL: Continue starting dose of amino acids and submit a urine sample for serotonin and dopamine assay.

URINARY SEROTONIN AND DOPAMINE PROCESSED: Laboratory testing reported out 5 business days after submitted. One day later (if requested) the medical consult interpreting results is reported out. (While not required, the medical consult report is most highly recommended.)

REVIEW RECOMMENDATION AND ADJUST AMINO ACIDS

FOLLOW UP WITH THE PATIENT IN ONE WEEK

RND SYMPTOMS UNDER CONTROL: Continue on the first adjusted dose of amino acids and set a follow-up visit in 1 week.

RND SYMPTOMS NOT UNDER CONTROL: Repeat cycles until symptoms are under control OR serotonin and dopamine are BOTH in their phase 3 optimal range (whichever comes first).

Amino acid formulas required for initiation of testing

Properly placing the system into the competitive inhibition state requires specific amino acid formulas.

Call DBS labs at 877-476-7229 for access to the amino acid formulas required for testing.

Due to patent licensing and quality assurance considerations, DBS Labs only performs lab testing on samples generated from patients taking properly licensed amino acids that meet QA standards.

THE VISIT ONE WEEK AFTER THE AMINO ACID DOSING IS CHANGED

It takes 3 to 5 days for serotonin, dopamine, and the amino acids to stabilize (reach equilibrium) each time there is a start or change in dosing values. The patients need to be seen in follow up 7 days after a dosing change. When seen in clinic, the proper question to ask the patient is, "How were your RND symptoms yesterday?" Note that yesterday was day six since the amino acid dosing was changed. If RND related symptoms were under control "yesterday," continue the amino acid dosing value, do not obtain a urine sample, and follow up in one week. If RND related symptoms were present "yesterday," continue the amino acid dosing value and submit a urine sample for serotonin and dopamine MTO analysis.

When symptoms or dysfunction involve low or inadequate serotonin, dopamine, norepinephrine, and epinephrine levels, a relative nutritional deficiency exists.

Basis Renal Monoamine Science

1. Serotonin and catecholamines do not cross the blood-brain barrier.
2. Urinary serotonin and dopamine are not simply filtered by the kidneys then excreted in the urine.
3. In patients not suffering from a hyperexcreting tumor the serotonin and dopamine found in the urine were synthesized by the kidneys.
4. Urinary serotonin and catecholamines have not been in the central or peripheral systems.
5. There is no direct relationship between amino acid dosing and urinary serotonin and dopamine levels.
6. Simply determining if the serotonin and dopamine levels in the urine are high or low is of no value if phase determination is not performed simultaneously in the competitive inhibition state (see page 2 for definition).
7. Serotonin and dopamine levels found in the urine are a function of transporters Organic Cation Transporters in the kidneys.
8. Urinary assays in the competitive inhibition state represent serotonin and dopamine not transported by the OCT2 out of the proximal convoluted renal tubule cells into the system.

Relative Nutritional Deficiency Testing Protocols

AMINO ACID DOSING REQUIREMENTS FOR VALID MTO (MONOAMINE TRANSPORTER OPTIMIZATION) TESTING AND ANALYSIS

The following amino acid dosing values need to be started one week prior to obtaining the first test (collection of first urine sample) on the proceeding page.

General Adult Protocol (may be used with all adults)

1. 4 pills NeuroReplete in the AM and 4 PM
2. CysReplete 2 pills 3 times a day with first dose at noon
3. Obtain urine sample and submit for serotonin and dopamine analysis in one week if symptoms are still present

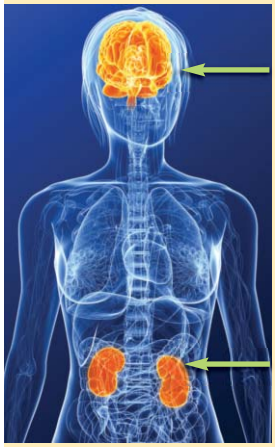
Pediatric Protocol

1. 2 pills NeuroReplete in the AM and 4 PM
2. CysReplete 1 pill 3 times a day with first dose at noon
3. Obtain urine sample and submit for serotonin and dopamine analysis in one week if symptoms are still present.

L-dopa Protocol

1. 4 pills D5 in the AM and 4 PM
2. CysReplete 2 pills 3 times a day with the first dose at noon
3. In one week continue the initial amino acid dosing and start D5 Mucuna 40% 2 pills 3 times a day
4. One week later obtain a urine sample as submit for serotonin and dopamine analysis.

Synaptic serotonin and dopamine levels are controlled primarily by the OCT 2 reuptake transporters located on the pre-synaptic neurons. MTO analyses and determines the status of the OCT2 then allows the physician to establish optimal levels of serotonin and dopamine in the synapse as encoded in on the OCT2.



Determining the functional status of the OCT2 in one place of the body determines the OCT2 status everywhere else in the body.

Determine the functional status of the transporters that regulate synaptic serotonin and dopamine levels and you have the key to optimal.

When managed properly there is no reason that the amino acids need to be permanently stopped!

CRASH COURSE

- **ORIENT THE PATIENT PROPERLY** (See orientation page 6)
- **START AMINO ACIDS** (See protocols to the left)
- **SUBMIT LAB SAMPLE IN ONE WEEK** if still with symptoms
- **FOLLOW MEDICAL CONSULT RECOMMENDATIONS** for amino acid dosing changes
- Know how to **MANAGE SIDE EFFECTS PROPERLY**
- **KNOW WHEN TO OBTAIN A PHYSICIAN- TO-PHYSICIAN CONSULT (877-476-7229).**
  1. When the desired results are not obtained
  2. Problems are encountered that do not respond to attempts to manage them in the clinic
  3. Any problem relating to the patient

Physician-to-physician consult: 877-476-7229 | Amino acids approved for testing: 877-476-7229

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READ ALL INSTRUCTIONS AND REVIEW MATERIALS IN KIT BEFORE COLLECTION.

1. 1 specimen name/date/time label
2. 1 urine collection cup
3. 1 urine transport tube
4. 1 pipette for transferring urine into transport tube
5. 1 lab requisition form
6. 1 resealable bag
7. 1 gauze wrap to wrap specimen tube

WARNING: If you missed even one dose of pills in the week prior to testing **DO NOT COLLECT A URINE SAMPLE** since missing pills is the leading cause of an invalid test being submitted.

WARNING: If you have had a major stressor the day of collection such as a car accident, unexpected death in the family, unexpected crisis, etc., do not collect a sample. Wait one to two days afterwards to collect a sample. Abnormal stress can lead to abnormally high neurotransmitters in the urine.

COLLECTION AND HANDLING INSTRUCTIONS

MOST IMPORTANT

1. Empty bladder 1 to 2 hours before collecting urine sample then drink one 16 oz glass of water.
2. **COLLECTION TIME IS CRITICAL:** Collect the sample **approximately 5 to 6 hours before bed time**. Normally this is just before you take your 4 or 5 PM amino acid dosing. Contact your caregiver if you need clarification on this.
3. Begin to void and collect the mid-stream sample of urine.
4. Transfer urine sample into transfer tube with pipette provided within 1 to 2 minutes of collection.
5. Store the sample at room temperature, do not store specimen in temperatures higher than 120 degrees Fahrenheit.

Fill out name/date/time label and apply directly to the specimen tube.

Unlabeled specimens will not be processed.

Return specimen with the FedEx shipping materials supplied.

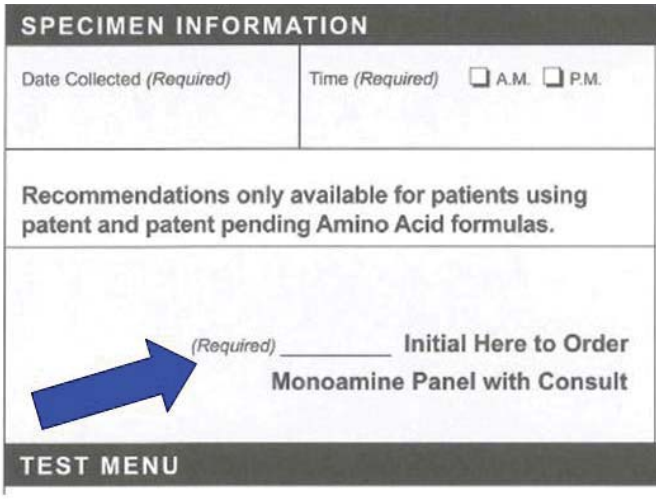
RETURN INSTRUCTIONS

1. Wrap sample tube in gauze pad provided and place in the small resealable bag.
2. **Completely fill out patient information on requisition form.**
3. Place specimen/ tube and the patient information form in the box provided then place in the FedEx clinic pack. Be sure to seal the top and apply billable stamp to the clinic pack.
4. Take the clinic pack to a FedEx collection box. If you do not have a FedEx collection box close by, call the FedEx 800 phone number to schedule a pick up.

FORMAL MEDICAL CONSULTS from licensed medical doctors under HIPAA guidelines available free of charge

Need help integrating this testing into other aspects of patient care? DBS Labs has arranged for licensed medical doctors to be available for medical consult free of charge. **Call 877-476-7229 to obtain a free medical consult.**

Ordering a free consult at the time lab testing is ordered. The patient information card that is required with each sample submitted to the lab has the following area in the lower left that needs to be initialed to obtain a medical consult analyzing the transporter phase along with subsequent need recommendations. This consult is subject to all of the rules and considerations of HIPAA.



When to get a testing consult

- Whenever urine samples are submitted in order to determine transporter phase analysis.
- Any time it would appear that the patient needs to permanently stop taking the amino acids obtain a medical consult. If managed properly, there is no reason to stop the amino acids permanently.
- When lab testing results or recommendations do not add up or there is a marked deterioration in the patient's nutrition-related symptoms after the recommended dosing change is put in place, a medical consult to discuss the clinical history would be beneficial.
- Whenever there is a question regarding the patient's care and there is not a firm answer available, call for a medical consult.
- Even with tens of thousands of tests under our belt not all problems are straightforward. Bottom line: two heads are better than one. Utilizing the medical consult to formulate a plan of action is the best approach.
- Since the consult is free, if the patient is unhappy or not doing as expected, call for a consult.

MORE THAN EIGHT TESTS, IT'S FREE

In evaluating the patient's relative nutritional deficiency status, if more than eight tests are required for stabilization, subsequent testing is free. This is contingent on the patient having gotten the first eight tests in a timely manner. For example, if three to six months elapse between tests, the clock will be reset. After eight more tests, any additional tests are free. Once the patient is stabilized, routine testing such as yearly follow up will once again be charged.

The reason for this policy is that most patients are stabilized with four to six tests. Free testing helps manage the risk of dropping out of care prior to stabilization. The second reason is that patients who require more than eight tests for stabilization are the most difficult.

For more information on all the details of "more than eight tests are free," call 877-476-7229.

One of the more prominent problems associated with testing is lack of follow through. Once the first urine sample is submitted for MTO (monoamine transporter optimization) there should be a firm commitment to finishing testing from both the patient and caregiver. The goal needs to be obtaining the urinary serotonin and dopamine in the phase 3 therapeutic ranges or stabalized nutrition, **whichever comes first.**

NOTHING IS INTUITIVE

On the surface the chemistry of serotonin and dopamine synthesis may seem simple and straightforward, but it is not. MTO (monoamine transporter optimization) research has disproven many of the commonly held ideas regarding serotonin and catecholamines (dopamine, norepinephrine, and epinephrine)

For example, if the patient becomes anxious after starting the amino acids, there may be a tendency to blame the L-tyrosine when in fact the problem is the balance between serotonin and dopamine precursors. The patient may be taking the proper level of tyrosine but not have enough 5-HTP as the cause of the problem. Achieving the correct balance of the neurotransmitters by properly balancing the precursors addresses the problems. MTO is the only way to optimize serotonin and dopamine transport in the system. If you are experiencing a problem, call for a consult.

PATIENT ORIENTATION: **THE FIRST VISIT**

Prior to starting the amino acids required for testing, all patients need to undergo an orientation.

#1 – At the first visit all patients need to be instructed as follows: **"If there are any problems in the first week, stop the amino acids until you get back to the clinic and I will instruct you on what to do."** Failure to properly orient patients at the first visit will result in patients dropping out of care if problems such as "GI upset on startup" (see the right column) are experienced in the first week of treatment.

#2 – **Return to clinic in one week** for evaluation and collection of the test sample.

#3 – **Prepare the patient for the** duration required to achieve optimal balance of nutrients and neurotransmitters. Patients need to be very clear that this optimal time only applies when weekly visits are in place. Missing weekly visits decreases the utility of testing by increasing time to the laboratory goal point.

#4 – **Take the first dose of CysReplete at noon.** The reason for this is that 20% of patients experience GI upset if CysReplete is taken first thing in the AM. If the patient happens to take the CysReplete in the AM and there is no GI upset, the first dose of the day can be continued in the AM.

#5 – **Instruct the patient that it may take 3 to 5 days** for the full effects of the start or change in amino acid dosing values to be observed.

#6 – **Instruct patients on the consequences of improperly taking the amino acids required for testing.** In some patients, missing one or more dosing values of amino acids may lead to the return of RND related symptoms for 3 to 5 days until equilibrium is once again established. A missed pill is equivalent to a dosing change and prolongs or eliminates the possibility of arriving at balance when doses are missed frequently.

PRESCRIPTION DRUG SIDE EFFECTS

THE PROBLEM: The recommendation is to leave all drugs in place when starting the amino acids. Side effects that are not associated with the amino acids may occur in 3% to 5% of patients while starting or changing the amino acid dosing.

MANAGEMENT: Management is to approach the event like a drug side effect. DO NOT stop the amino acids. Tapering or stopping the drug that is causing the side effect is proper management.

GI UPSET ON START UP

THE PROBLEM: Approximately 1% to 2% of patients (higher in some medical practices where patients have been exposed at a higher rate to drugs that deplete neurotransmitters) experience GI upset or nausea on starting the 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: The patients who are most depleted of neurotransmitters experience GI upset or nausea on starting the amino acids. ***These are the very patients who need the amino acids the most.***

MANAGEMENT: Restart the amino acids taking only one pill of NeuroReplete or D5 at bedtime. Bedtime is when the patient is ready to get in bed and immediately go to sleep. If the patient can fall asleep within 20 minutes after taking the one pill of NeuroReplete, there should be no problems with GI upset. After 3 or 4 nights with no GI problems increase the NeuroReplete to 2 pills at bedtime. When the patient is able to take 2 pills at bedtime with no problems, start 1 pill in the AM then increase to two pills after 3 or 4 days of no problems. In adults, when the patient is taking 2 pills of NeuroReplete twice a day, submit a urine sample for transporter evaluation. GI upset on startup in pediatric patients is virtually unknown.

GI UPSET CAUSED BY FROM CARBOHYDRATE INTOLERANCE

THE PROBLEM: Once the proper dosing values of the amino acids have been established, patients may experience transient nausea lasting 45 to 60 minutes periodically during the day. The etiology of this problem is distinctly different than "GI upset on start up" as discussed above.

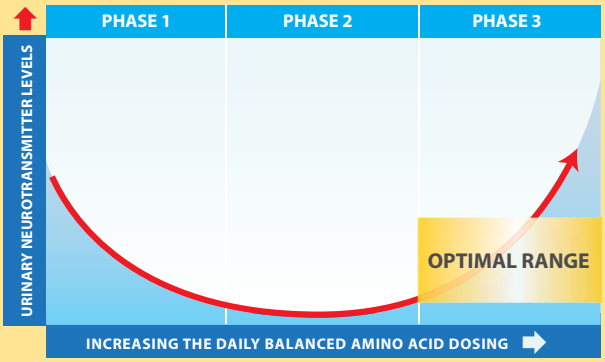
THE CAUSE: With optimization of neurotransmitter transporters, the way the body reacts to specific carbohydrates may change causing nausea.

MANAGEMENT: Usually only one food needs to be changed. Most of the time, it is a bread, cereal, or noodle that needs to be changed. Examples of effective management include: 1) changing from white to whole wheat bread; 2) changing from one type of noodle to another; or 3) changing from one cereal to another, for example changing from Wheaties to Shredded Wheat. At times identification of the food can be difficult. One case of carbohydrate intolerance was tracked down to the breading on chicken eaten with most lunches.

PARADOXICAL REACTION

THE CAUSE: The exact cause of paradoxical reactions is unknown, but it is known that there is a dosing range in certain individuals within which they do occur.

MANAGEMENT: When a paradoxical reaction is identified, it is an indication that the amino acid dosing value needs to be increased, at which point the paradoxical symptoms will resolve in one to two days. If the dose is lowered in hopes of increasing the dosing values slowly, the patient's suffering will be unnecessarily prolonged as the patient is subjected to the dosing value range where symptoms occur for a prolonged period of time. **THIS IS THE PLACE FOR THE CONSULTATION TO DETERMINE THE DOSING CHANGE NEEDED.**



Urinary serotonin and dopamine found in the urine is newly synthesized in the proximal tubule cells of the kidneys. Under normal circumstances it does not represent serotonin and dopamine that have been filtered by the kidneys and placed directly in the urine.Once synthesized the new serotonin and dopamine are transported by the basolateral monoamine transporter (OCT2) to the interstitium then ultimately to the renal vein and system. Serotonin and dopamine not transporter basolateral monoamine transporter is transported by the apical monoamine transporter (OCTN2) ending up on the final urine as waste. Proper interpretation of urinary serotonin and dopamine levels determines the functional status of the basolateral monoamine transporter.

HEARTBURN (PYROSIS)

THE PROBLEM: Intense substernal or epigastric burning or nausea after taking the pills.

THE CAUSE: When the veggie caps are simply gulped down with some water the surface does not liquefy properly causing the pills to stick in the esophagus and dissolve, at which time an intense substernal and/or epigastric burning is experienced.

MANAGEMENT: Hold the pills in the mouth with water for 10 to 15 seconds before swallowing so that the capsule surface starts to liquefy and slides down easily.

DIZZINESS

THE PROBLEM: Dizziness (vertigo) may be caused by many different things when taking amino acids. As with paradoxical reactions, in many cases it is an indication to increase the amino acid dosing.

THE CAUSE: While complaints of dizziness may have many etiologies, dizziness associated with inadequate amino acid dosing is responsive to food intake. If the patient complains of dizziness that resolves after eating a small amount of carbohydrate, such as a candy, cookie, pastry, etc., it is a carbohydrate-dependent vertigo which can develop during amino acid treatment.

MANAGEMENT: Management of "carbohydrate-dependent vertigo" involves increasing the amino acid dosing to the level where symptoms will resolve in one to two days. Any patient taking amino acids with complaints of dizziness needs to be properly evaluated for "carbohydrate-dependent vertigo". A consultation will help to decide the dose change.

WHEN AMINO ACIDS STOP WORKING

THE PROBLEM: The patient's symptoms relating to relative nutritional deficiency are under control and then it appears that the pills stopped working and RND symptoms return.

THE CAUSE: Missing one or more doses of amino acids can cause RND symptoms return. It then may take three to five days for RND symptoms to get back under control once the pills are taken correctly. If the patient misses one pill dosing every three to four days multiple times, it may appear that the amino acids have stopped working for a prolonged time.

MANAGEMENT: In 99% of patients for whom the pills stop working it is a compliance issue relating to taking the pills properly. Have the patient journal (write down) all pills taken for 7 to 10 days. After journaling if the patient's RND symptoms are not under control, submit a urine sample for transporter assay. Only 1% of patients experience a change in amino acids dosing needs during management and retesting can manage this problem.

VALIDATING THE JOURNAL is not simply having the patient write down all pills taken then asking the patient if the journal was completed. ***In order for the journal to be validated it needs to be reviewed by the caregiver as an integral part of the visit.*** Most problems identified through journaling occur when the caregiver reviews the journal. Simply asking the patient over the phone, "Did you complete your journal?" is of no value. The patient needs to physically bring the journal to the clinic for review. Experience has shown that if a patient shows up at the clinic claiming to have journaled all week but did not bring the journal to the clinic, in most cases the patient did not journal. Patients who take the time to journal do not forget to bring their paperwork to the clinic for their visit.

HYPERSOMNOLENCE

THE PROBLEM: After starting the amino acids a patient complained of excess sleepiness to the point of having problems staying awake at work or during other daily activities.

THE CAUSE: In general, these patients were suffering from poor sleep (chronic insomnia) prior to treatment and have a "sleep debt" that needs to be repaid prior to feeling optimal again.

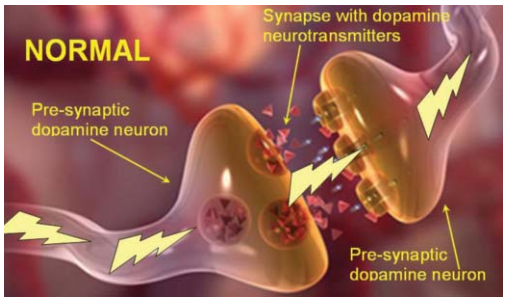
MANAGEMENT: The first thing to do when complaints of excessive tiredness are encountered is to take a medical history to determine whether the cause is an imbalance in the amino acids or if the patient is suffering from a sleep debt due to chronic insomnia that needs to be repaid. In patients with very poor sleep prior to treatment (3 to 4 hours per night), stop the amino acids and restart them on a Friday if the patient has the weekend off, telling the patient to sleep all weekend. If sleep was not a problem prior to treatment, cut the amino acid dosing in half, then submit a urine sample for MTO (monoamine transporter optimization) in order to determine the proper levels of amino acids needed.

TAKING AMINO ACIDS WITH FOOD

The amino acids recommended prior to testing and for management of the relative nutritional deficiency resolution can be taken with or without food. The status of food does not affect potency, absorbability or outcomes.

Low or inadequate serotonin and/or dopamine levels are not a disease; rather it is a nutritional issue. Our testing can help you determine the patient's nutritionally driven transporter function status.

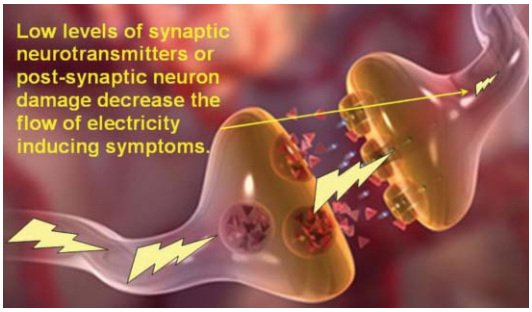
Monoamine neurotransmitter levels (concentrations) in the brain and peripheral system are primarily controlled by transporters.

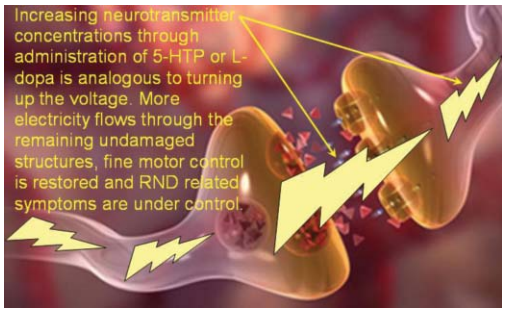


THE PROBLEM

Low or inadequate levels of one or more of the centrally acting monoamine neurotransmitters (serotonin, dopamine, norepinephrine, and epinephrine) are caused by a relative nutritional deficiency.

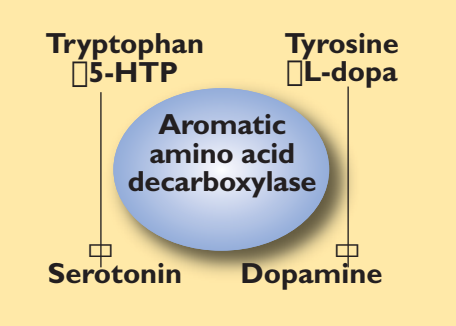
These neurotransmitters are synthesized from nutrients in the food. When neurotransmitter levels are not high enough a relative nutritional deficiency exists. One safe way to increase the total number of monoamine neurotransmitters in the brain is through administration of properly balanced amino acid precursors.

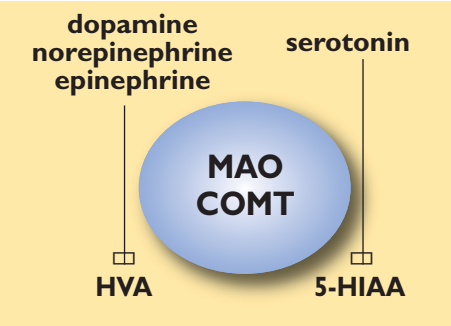


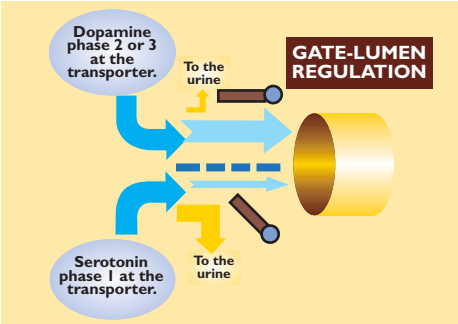


Simply giving some amino acids may do more harm than good. Monoamine Transporter Optimization (MTO)™ is a revolutionary approach that determines the status of the transporters in order to define optimal amino acid dosing values required for optimization of serotonin and catecholamines (dopamine, norepinephrine, and epinephrine).

How improperly balanced amino acids deplete monoamine neurotransmitters







SYNTHESIS IN COMPETITIVE INHIBITION

The same enzyme, L-aromatic amino acid decarboxylase (AAAD), is responsible for synthesis of serotonin and dopamine. If an environment is created in the competitive inhibition state where the amino acid precursors of one system dominate the AAAD, decreased synthesis and depletion of the non-dominant system occur.

METABOLISM IN COMPETITIVE INHIBITION

Both serotonin and dopamine are metabolized by the monoamine oxidase (MAO) enzyme system. A significant increase in levels of one system increases MAO activity and causes domination of the enzyme, leading 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.

Medical consults under HIPAA: Please call the office at 877-476-7229 when ever a medical consult is required. Occasionally physicians obtain the private cell phone number of physicians providing consults and call them direct. Calling the office instead of the private call phone facilitates a proper consult where a written recommendation is generated and on file. It also facilitates prompt response to any needs that arise on the phone.

Pregnancy: there are no studies which demonstrate that the amino acids required for testing are safe in pregnancy nor are there any studies demonstrating they are harmful. In this light, the recommendation is to not take the amino acids during the first trimester (13 weeks) of pregnancy.

In situ monoamine transporter functional status assay™

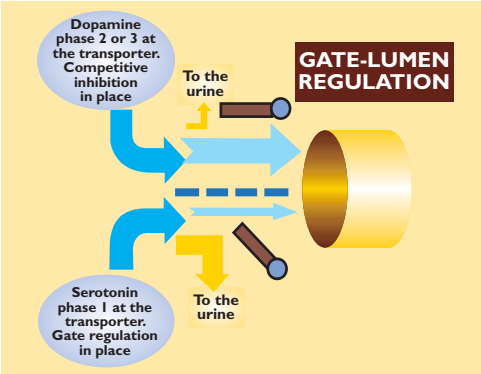
MONOAMINE TRANSPORTER OPTIMIZATION (MTO) ™
ORGANIC CATION TRANSPORTER FUNCTIONAL STATUS DETERMINATION™

Optimization of the administration of centrally acting monoamines and their precursors™

The intercellular and extracellular concentrations of serotonin, dopamine, norepinephrine, and epinephrine are primarily controlled by monoamine transporters. These neurotransmitters and their precursors do not move freely in and out of cells to places where they are synthesized and metabolized; transporters are required.

Since 2004, daily review of thousands of urinary monoamine laboratory assays from patients taking and not taking serotonin and dopamine amino acid precursors revealed a previously unknown inflection in the laboratory response. This three phase inflection of urinary serotonin and dopamine was previously unknown and had never been published in the scienctific literature (see Figures 3 and 4).

The etiology of the three phase inflection (inverse, no, direct) took seven years to unravel. This three phase response is the result of the Organic Cation Transporter Type 2 (OCT2) high affinity transport system. Interpreting the status of this system reveals a unique opportunity into functions of the brain which are controlled by the same transporters.



The "dual gate lumen model" published in 2010 serves as the foundation for MTO.™

FIGURE 3: The three phase serotonin response™

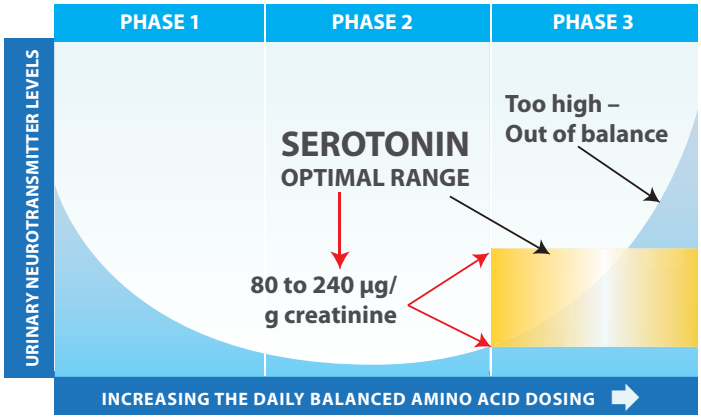
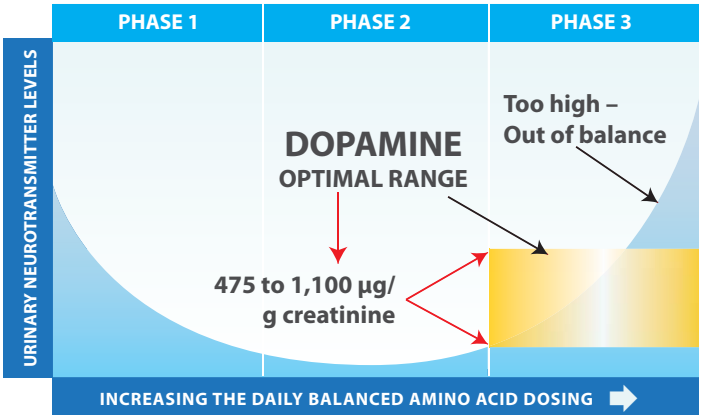


FIGURE 4: The three phase dopamine response™



When serotonin and dopamine amino acid precursors are administered, proper interpretation of urinary assays leads to determination of OCT2 function throughout the body. The OCT2 and high affinity transporters of the brain are primarily responsible for synaptic serotonin and dopamine concentrations.

The primary forces responsible for establishing monoamine neurotransmitter levels throughout the body are synthesis, metabolism, and transport. Transport dominates with its control and regulation over synthesis and metabolism.

The first step in this relative nutritional deficiency management protocol is the simultaneous administration of serotonin and dopamine amino acid precursors in dosing values great enough to place the system into the competitive inhibition state. Then, one week later a urine sample is obtained, monoamine assays are performed and MTO interpretation is done. This enables a proper decision on the modification of the amino acid dosing values in order to achieve both serotonin and dopamine in their phase 3 optimal ranges.

The serotonin phase and the dopamine phase are independent of each other. For valid interpretation to occur, both serotonin and dopamine precursors must be simultaneously administered.

OCT2 found primarily in brain and kidneys

Identical homologous

Encoding of transporters

MTO interpretation™

The goal of testing is to establish both the serotonin and dopamine in the phase 3 optimal ranges. The process of interpreting the status of the OCT2 in order to prescribe changes is not something that can be accurately performed in clinic. Computer-assisted analysis is required to establish the phase of both serotonin and dopamine. Use of this information enables accurate determination of the proper amino acid dosing value changes needed.

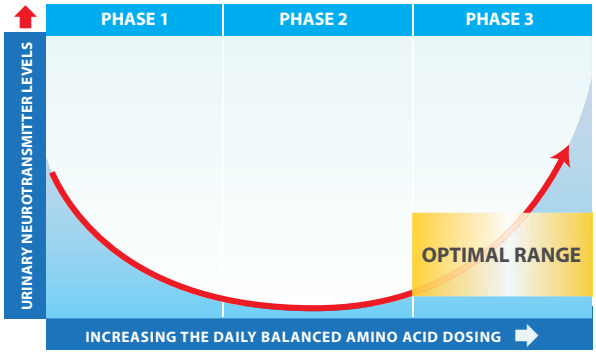
When serotonin and dopamine urinary testing is ordered, the patient information card found in each kit has a check box that indicates a request for a medical consult. This consult by licensed medical doctors offers the determination of phase and transporter status and makes amino acid dosing change recommendations. The medical consult is free of charge and available only to licensed health care providers.

Basic MTO laboratory interpretation

Goal: Relief of RND related symptoms or both serotonin and dopamine in the phase 3 optimal ranges

OPTIMAL RANGES

Serotonin = 80 to 240 µgr / gr cr
Dopamine = 475 to 1,100 µgr / gr cr

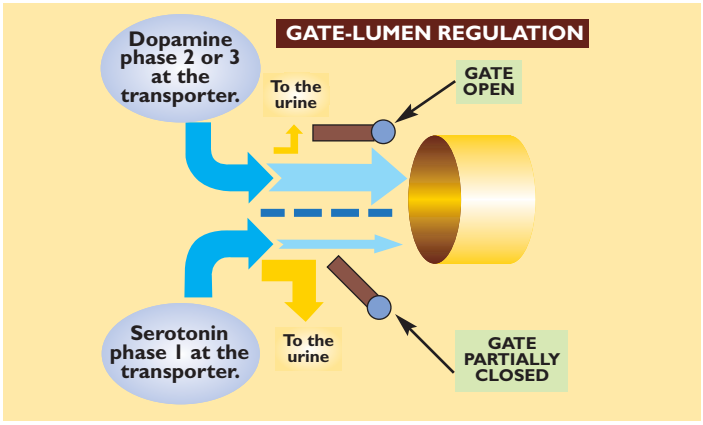


PERSPECTIVE

Interpretation of these labs IS determination of the functional status of the OCT2 transporters in the body. This IS NOT a simple lab determination where the lab is glanced at and there is a determination if the results are simply high or low.

Once the serotonin and dopamine values are reported by the lab the phase that each are in needs to be determined.

Phase analysis allows for the status of the transporter entrance gates and the transporter saturation to be determined.



	GATE	LUMEN
PHASE 1	Partially closed	Unsaturated
PHASE 2	Open	Unsaturated
PHASE 3	Open	Saturated

The Organic Cation Transporters Type-2 (OCT2) of the kidneys are identical to the OCT2 found on the pre-synaptic neurons of the brain, which carry out reuptake of serotonin and dopamine. Determine the status of transporters in one place and you have just determined the OCT2 status everywhere else they exist.

SYNAPSES OF THE BRAIN

Phase 1 – Serotonin and/or dopamine levels in the synapses are not high enough. The serotonin or dopamine entrance gate is partially closed restricting reuptake so that synaptic neurotransmitter levels increase. As the synaptic levels increase, the gate gradually opens until it is fully open.

Phase 2 – There is now adequate serotonin and dopamine in the synapse, but the system as a whole is not functioning optimally. The pre-synaptic vesicles which contain neurotransmitters waiting to be excreted into the synapse are not fully charged, meaning that optimal response to changes in synaptic neurotransmitter requirements may not be implemented.

Phase 3 – The synapse and the pre-synaptic vesicles now have optimal levels of neurotransmitters. Both serotonin and dopamine need to be established in the optimal ranges (Serotonin phase 3: 80 to 240 µg / g creatinine; Dopamine phase 3: 475 to 1,100 µg / g creatinine). If both serotonin and dopamine are in phase 3 and one is above the optimal range, it will dominate and compromise the other system in synthesis, metabolism, and transport.

In the Kidneys

Phase 1 – With the entrance gates partially closed there is increased excretion to the urine. This is protective and prevents flooding of the peripheral system by the serotonin and dopamine that have been newly synthesized by the kidneys while synaptic levels are being increased.

Phase 2 – The gate is open and the peripheral system is now charging.

Phase 3 – The peripheral system is charged and the excess serotonin or dopamine is being excreted appropriately by the kidneys.

Expertise required for interpretations

While understanding a few basic rules will lead to some basic insight into determination of transporter status, there is a huge learning curve. Properly interpreting the phase status is analogous to the radiologist performing radiologic procedures, you can under stand the basics but without a lengthy residency you will not master the subject.

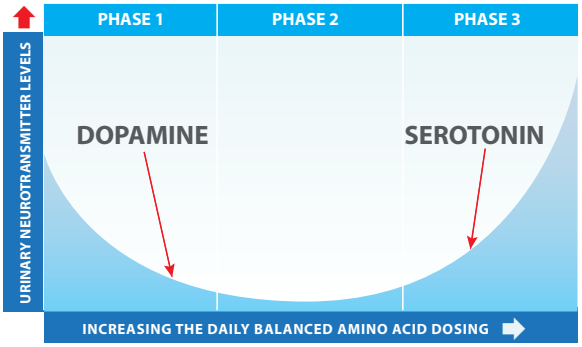
The basic rules

#1 – serotonin and dopamine are never in phase 1 at the same time.

#2 – when L-tyrosine is given with 5-HTP dopamine will never be over 475 µgr / gr cr phase 3.

Example 1: Only L-tyrosine and 5-HTP are being administered therefore the dopamine has to be phase 1 and the serotonin is phase 3 under the two rules above.

Serotonin µgr / gr cr	Dopamine µgr / gr cr	5-HTP mg	L-tyrosine mg
698 phase 3	578 phase 1	300	3,000



Rule #3: adding or subtracting a serotonin or dopamine precursor will affect both as if precursor of each has changed

Serotonin µgr / gr cr	Dopamine µgr / gr cr	5-HTP mg	L-tyrosine mg	L-dopa mg
698 phase 3	578 phase 1	300	3,000	0
998 phase 3	345 phase 2	300	3,000	120