

FROM A NEURORESEARCH WRITING

NEUROTRANSMITTER TESTING GUIDELINES

By: Marty Hinz, MD NeuroResearch

[PDF version >>> NEUROTRANSMITTER TESTING GUIDELINES](#)

INDICATIONS FOR NEUROTRANSMITTER TESTING

1. Establish a proper therapeutic range for neurotransmitter in treatment.
2. When high dose amino acid therapy is being considered (above 900mg 5-HTP and 5,000mg tyrosine).
3. In patients who begin to struggle during treatment.
4. Periodically (every six months) to insure that neurotransmitter function remains optimal while on amino acid therapy.

OVERVIEW

In using neurotransmitter testing in support of treatment, it is important to keep your eye on the ball. In medicine, laboratory testing is used in the treatment of patients primarily for two purposes:

1. To assist in making or confirming a diagnosis.
2. To assist in treatment.

Just as with any medical lab test, if you cannot document the reason for it in your medical record, you probably do not need it.

After much consideration and work, I would put forth the following considerations on indications for neurotransmitter testing in the treatment of patients with amino acids.

Neurotransmitter testing is of no value at initiation of treatment. Hyperexcretion of neurotransmitters in a significant number of patients is the problem. This is a state where the kidneys are excreting excess amount of neurotransmitters and the urinary neurotransmitter levels do not correlate with the systemic levels of neurotransmitters. Once treatment is underway with amino acids this problem no longer appears to be a consideration.

Neurotransmitter testing is not proven as a diagnostic tool to make a diagnosis in patients, even in those patients where there is a high correlation with hyperexcretion of neurotransmitters such as children with ADHD. Establishing a diagnosis should be done under traditional medical guidelines. For example, every physician knows that when a patient presents with depression you should check a TSH and hemoglobin to insure that you are not missing a hypothyroidism or anemia. With a normal TSH and hemoglobin you have

confirmed the diagnosis, ruled out other disease and amino acid therapy or other treatment modalities may be initiated.

In the weight loss patient, a neurotransmitter test is not indicated since you already have your diagnosis and are committed to treatment. There indeed are some indications for neurotransmitter testing at the initiation of treatment that will be released next month, but these are mainly in the areas where the diagnosis may be left open to question.

Neurotransmitter testing is of no value prior to initiation of treatment in selecting the amino acid doing that the patient should be treated with. The reason for this is quite complex and taught in depth at the NeuroResearch seminars. A brief over view is as follows. The important thing in treating patients is to use the amino acid precursors of the catecholamine system (dopamine, norepinephrine, and epinephrine) in proper balance with the amino acid precursors of the serotonin system. Our work has shown that giving 5-HTP alone or with too little catecholamine precursor can lead to depletion of the catecholamines. Conversely giving L-dopa or L-tyrosine alone or with too little 5-HTP can lead to depletion of serotonin. The goal of treatment is to use properly balanced amino acids in treatment to obtain therapeutic levels of neurotransmitters. By attempting to change the optimal dosing ratios for amino acids that NeuroResearch has defined in the treatment of only distracts from results and leads to sub-optimal group response.

Through our research and literature review we know that L-dopa in treatment depletes S-adenosylmethionine (S-AdoMet). S-AdoMet and cortisol are the two critical components in the synthesis of epinephrine from norepinephrine. S-AdoMet is the one carbon methyl donor for chemical reactions in the body. We have also found that L-tyrosine can cause depletion of S-AdoMet and all the problems associated with L-dopa treatment, but on a smaller scale.

So the question becomes, "How do you prevent L-dopa related depletion problems?" NeuroResearch for the answer to this:

1. Give all patient 4,500mg of cysteine per day with proper levels of cofactors.
2. Use L-dopa and L-tyrosine in proper balance with serotonin precursors.
3. Monitor long-term amino acid patients every 6 months to insure that neurotransmitter levels are optimal paying close attention to the epinephrine levels.

For the most part, the main indication for neurotransmitter testing is with cases where the patient is:

1. Establish a proper therapeutic range for neurotransmitter in treatment.
2. When high dose amino acid therapy is being considered (above 900mg 5-HTP and 5,000mg tyrosine).
3. In patients who begin to struggle during treatment.
4. Periodically (every six months) to insure that neurotransmitter function remains optimal while on amino acid therapy.

ESTABLISHING A THERAPEUTIC RANGE

Once the patient has started treatment, neurotransmitter levels can be titrated with pinpoint accuracy using neurotransmitter testing. With the data we obtained from over 200 clinics around the U.S. we know that neurotransmitter levels that are too low cause problems. The other side of the coin is that we have identified instances where neurotransmitter levels that are too high from excess use of amino acids actually causes

decreased group performance. With this in mind the goal should be to establish neurotransmitter levels in, “The therapeutic range” during treatment.

Therapeutic Ranges

	Dopamine	Serotonin
Non-weight loss	300-500	800-1,200
Weight loss patients	400-600	1,200-2,400

HIGH DOSE NEUROTRANSMITTER TESTING

“High dose” is defined as amino acid dosing where the daily amino acid intake is greater than 900mg per day of 5-HTP or 5,000mg of tyrosine. This is known as the “8 and 8” level of dosing (greater than 8 NeuroReplete or D5 and 8 RepleteExtra or D5 Extra per day). Getting neurotransmitter testing on patients who are not responding fully at the “8 and 8” level of dosing will confirm that the patient does indeed need more amino acids in order to establish a clinical response and to verify that you will not be overloading the system by prescribing a dosing level higher than the “8 and 8” level.

TESTING IN THE STRUGGLING PATIENT

In the patient that is struggling after doing well for several weeks or months on amino acid therapy, the first step to evaluation IS NOT to get neurotransmitter testing, but to have the patient journal and write down all the pills taken for one week to insure that the patient is not missing any doses. In many cases, if a patient misses a dose or two the clinical benefits will no longer be seen. It will take 3 to 5 days of not missing a dose before the clinical response is once again apparent. If the patient does return in one week and has taken the pills properly and is still struggling, then it is time to obtain a neurotransmitter test to assist in clinical decision-making.

NEUROTOXICITY PROTOCOL

In general neurons do not function as a single unit, they function as groupings of neurons throughout the body known as nerve bundles. Nerve bundles, (groupings of neurons) are critical to maintaining life, if we relied on a single neuron for regulation of bodily functions and it became damaged and unable to do it’s job human beings would be in trouble quickly.

Example A is a simple illustration showing a bundle of 1,000 neurons each conducting one nannowatt of electricity. The illustration shows 1,000 nannowatts in and 1,000 nannowatts out of the neuron bundle.

Example A

Example B illustrates the effects of neurotoxicity that has damaged 500 neurons to the point of being non-functional, 1,000 nannowatts in 500 nannowatts out.

Example B

Herein lies the problem it is the net outflow of the neuron bundles that must be above a certain threshold in order for the system as a whole to be healthy. If neurotransmitter levels in the synapse are too low the output of the neurons is low and disease and illness develops. If the enough neurons of the bundle are damaged and the net outflow of the bundles becomes low enough disease and illness develops.

From a clinical standpoint disease and illness caused by low levels of neurotransmitters in the synapse and damage to the neurons of the bundles looks the same, neurotransmitter disease and illness. From a clinical standpoint the treatment is the same with the exception of group dosing as discussed below.

In our research the ability to differentiate the patients with illness due to low levels of neurotransmitters in the synapse from those that have a component of neurotoxicity came about through large-scale database research. In evaluation amino acid needs of patient to obtain the desired clinical response database research has shown that those patients with a history of taking the neurotoxin fenfluramine (a component of phen-fen) need significantly higher dosing of amino acids to obtain the desired clinical response in comparison to those that have no history of fenfluramine exposure. Other neurotoxins include amphetamine, ecstasy, heavy metals, pesticides, and a host of other things.

In order to obtain the proper clinical response in those patients who have been exposed to neurotoxins in the past neurotransmitter levels higher than normal must be established in the synapse thereby hyperexciting the remaining non-damaged neurons and increasing the output of the neuron bundle. Example C illustrates the effects of hyperexcitement of the neuron bundle with half the neurons damaged permanently by neurotoxicity in order to give a disease free state in the patient. By proper use of amino acids the levels of neurotransmitters in the synapse is increased above normal levels causing the electrical outflow of the neuron bundle to rise above the threshold needed to keep the patient and the system symptom free of disease, this is discussed more below.

Example C

THRESHOLDS

As based on thousands of clinical observations and clinical data there exists a threshold and if you look for it in the patients you become aware that it is well defined. This threshold is like a light switch it is either on or off. From a clinical standpoint the symptoms of disease are either present or not, or the neurotransmitter drugs are either working or not. Display of the threshold from a clinical standpoint is very easy to identify if you know what to look for. Patients who are doing well and have the symptoms under control that you are attempting to treat miss one or two doses of amino acids and the symptoms of their illness return. We have seen cases where the patient's dosing of amino acids was just above the threshold and by lower the daily dosing of pills by one pill caused the symptoms of the disease or illness to return. The awareness of the threshold and its importance in treating patients explains why patients as a group need such a diversion range of amino acid dosing from patient to patient in order to obtain relief of symptoms.

The amino acid dosing to raise neurotransmitter levels above levels needed to prevent symptoms of disease vary widely in patients. We have seen the rare patient who on two pills a day experience complete relief of symptoms and on the other end of the spectrum is the rare patient who needs four pills five times a day.

NEUROTOXICITY AND THRESHOLDS

For patients who eat even an optimal diet the body by way of biochemical feedback loops will regulate the amount of neurotransmitters produced. In the patients there is only a specific amount of neurotransmitters that will be produced at which point production of neurotransmitters is regulated and shut down in the body.

5-HTP and L-dopa bypass the biochemical neurotransmitter production regulation points and allow for us to establish catecholamine (dopamine, norepinephrine, and epinephrine) levels that are higher than normally produced in the body. This basic biochemical concept is very important to understand especially in the management of "system damage".

As the system becomes damaged through insult such as neurotoxicity, trauma, congenital problems, or anything that compromises the flow of electrical impulses from the bundles the neurotransmitter threshold in the synapse needed to keep the system symptom free rises. From the large amount of data and research we have done we know that in many patients with system damage need neurotransmitter levels established that is above those levels found normally in patient who simply take in tryptophan and tyrosine, both of which allow the body to produce neurotransmitters only up to a certain level.

PARKINSON DISEASE AS A PROTOTYPE

Based on work of neurologists in San Francisco in the mid-1980s the MPTP theory of Parkinson disease emerged. MPTP is a neurotoxin that is very specific in causing damage of the dopamine neuron of the substantia nigra of the brain. If enough of these neurons sustain

permanent damage through neurotoxic insult symptoms of Parkinsonism develop with one prominent feature being the “pill-rolling tremor”.

Since 1969 when L-dopa therapy became available in the U.S. patients with Parkinson disease have been treated with L-dopa. L-dopa increases the peripheral and central levels of dopamine above normal levels and as these levels increase the outflow of the undamaged dopamine neurons increases and the symptoms improve.

Several years ago we formulated the following theory. The serotonin system and the catecholamine system must both be functioning properly for the system as a whole to function properly. The serotonin system functions more like a light switch that is either on or off, whereas the catecholamine system functions more as a dimmer switch where the flow is gradually increased as you turn the switch up. The serotonin switch must be on and the catecholamine dimmer switch must be turned on full in order for the system to function optimally and disease free. The effects of L-dopa in Parkinsonism are a good illustration of the dimmer switch effects of the catecholamine system, as you increase the dosing of the L-dopa thereby increasing the systemic levels of dopamine they symptoms of the Parkinson disease resolve in a dose related manner and not in an on or off manner as is seen with those diseases that have a significant serotonin component.

In performing neurotransmitter testing on patients with Parkinsonism and other neurotransmitters diseases it is apparent that in treating a group of patients the only effective treatment is by establishing balanced neurotransmitter levels higher than the body will normally manufacture with tyrosine and tryptophan from the diet.

SYSTEM DAMAGE IS SYSTEM DAMAGE

Up until now we have discussed the effects of neurotoxic system damage with Parkinsonism being the prototype. There certain are many other neurotoxins, in this writing it is not important to discuss all the neurotoxins with their mechanism of action, but to simply realize that damage is damage and from a clinical standpoint it all looks the same, disease symptoms.

In talking about damage we almost overlooked the obvious, the patient with mechanical damage from injury. Very rarely do we discuss things that we do not have large amounts of clinical data on, but the reports we have received from physicians and patients relating to post traumatic head injury and other mechanical damage is so compelling we have included the following.

We have received numerous reports from physicians and patients indicating dramatic improvement of residual symptoms relating to post traumatic head injury. One physician at our Chicago seminar in August 2002 reported that he felt like he had been walking around in a fog for 5 years after an automobile accident where he sustained a close head injury. Almost immediately after starting the NeuroReplete formula he reported the fog had lifted and he had been doing well for the previous 3 months.

The point is that damage to the system is damage to the system be it from neurotoxins, trauma or otherwise. When the neuron bundles get damaged to the point that their outflow is no longer adequate to keep symptoms of disease at bay the patient suffers.

BOTH SYSTEMS MUST FUNCTION OPTIMALLY

For most patients proper use of tyrosine and 5-HTP can give proper clinical results, although the use of 5-HTP and L-dopa is also an alternative.

79% of over 600 patients not under treatment showed low levels of epinephrine on testing. The implications are not only that the neurotransmitter levels are not optimal, but that SAME and/or cortisol are not functioning proper either. We also know that BOTH the serotonin and the catecholamine system must be functioning properly for the system as a whole to be healthy and disease free.

If you simply give patients 5-HTP, tyrosine, or L-dopa you will not get optimal group results. For example, you can give all the 5-HTP you want to a patient with very low catecholamine levels and nothing will ever happen. It is only when you bring the catecholamine levels up in combination with the 5-HTP that you will see optimal group results. The same is true on the catecholamine end of things. You can give all the tyrosine or L-dopa you want to a patient but if they have very low serotonin levels you will get no clinical response until bring up the serotonin levels and address both systems properly. A proper balanced approach to the treatment of patient whereby both systems are addressed is the only way to get optimal group results in treatment.

TWEAKING NOT A SLEDGE HAMMER

From time to time we get questions asking, "Isn't increasing neurotransmitter levels dangerous, can it cause serotonin syndrome?" The answer to these concerns is, "no". Clinical experience, data, and laboratory testing have shown that we are merely tweaking the system and not sledge hammering it like drugs do.

Serotonin syndrome is mainly associated with the use of an MAO inhibitor and SSRI medication together. There are no reports of serotonin syndrome with amino acids. Furthermore, we are aware of research work that shows that amphetamines for example increase synaptic serotonin levels by 2,500 times. The laboratory test that we have performed show that neurotransmitter levels increase by only 4 to 10 times in therapy with amino acids. We are truly tweaking the system instead of sledge hammering it like drugs that cause serotonin syndrome do.

NO SUCH THING AS OPTIMAL

Over the last year the concept of "optimal neurotransmitter levels" came into this project. I never was truly comfortable with the concept, which basically stated that in a group of people there is an "optimal level" for neurotransmitters to be at within the defined, "normal range" of neurotransmitters. As research continued it became apparent that the concept of "optimal levels of neurotransmitters" is meaningless. There is such a vast difference in the therapeutic needs of neurotransmitter in the human population. System damage, neurotoxicity, and a host of other factors came into play which require neurotransmitter levels to be established higher than the normal range to allow the patient to be symptom free and in the process the concept of, "optimal in the therapeutic range" meaningless. The valid way of looking at neurotransmitters and proper treatment is, "What is the level needed to

keep the system functioning optimally and disease free?”, and not “What is the optimal level for a group of people independent of those that still have symptoms of disease and are not functioning optimally?”

L-DOPA AND SAME

So what is the recommendation for CysReplete? (Combination cysteine and selenium). The guidelines are as follows:

1. All patients taking Mucuna (L-dopa) and L-tyrosine need to take CysReplete.

Dosing of CysReplete is recommended as 2 pills three times a day (a total of 4,500 mg of cysteine per day). The clinical research we have done on the dosing needs of CysReplete in weight loss and other disease was unique and interesting. Patients given 2,250mg of cysteine a day reported that they felt they were doing better, but no objective clinical data from treatment effects could be seen until a daily dosing of 3,750mg a day was achieved and optimal group response occurred at the 4,500mg per day dosing level. I am sure giving less than 2 pills three times a day (4,500mg cysteine) is better than nothing but for optimal group benefit you need to give 2 pills three times a day (4,500mg cysteine).

Use of L-dopa as found in Mucuna, L-tyrosine to a lesser degree, and some prescription drugs lead to depletion of S-adenosylmethionine (SAME).

1. Long-term use of L-dopa is associated with development of the irreversible side effect of dyskinesias.
2. Dyskinesias generally develop at about 4 to 6 years into L-dopa therapy.
3. Dyskinesias are known to be associated with SAME depletion.
4. SAME is the single carbon methyl donor for all chemical methylation reactions in the body.
5. SAME is one of the two critical components needed by the body to turn norepinephrine into epinephrine.
6. Long-term use of L-dopa depletes epinephrine stores and compromises all of the other 41 major pathways in the body that depend on one carbon methylation.
7. Proper use of cysteine will prevent SAME depletion by L-dopa.
8. Monitoring of urinary epinephrine levels in patients on long-term L-dopa therapy will help to insure that the system continues to function properly.

We have a high degree of certainty that long-term use of L-dopa with proper intake of cysteine will prevent the irreversible side effect of dyskinesias. To keep you patient safe monitor neurotransmitter testing every six month pay special attention to the epinephrine levels.

HYPEREXCRETION

Hyperexcretion of neurotransmitters occurs primarily with the catecholamine system although it has been seen with the serotonin system as well. It is a phenomenon seen in patients starting treatment in which neurotransmitter testing was performed prior to starting the patient on amino acid therapy. Bearing in mind that the body on a normal diet without supplemental amino acid L-dopa or 5-HTP will only synthesize neurotransmitters up to certain level known as the “high end of the normal range” on neurotransmitter testing.

In patients with hyperexcretion the neurotransmitter found in the urine can be two to three times the “high end of the normal range”. Many times I have received calls from physicians saying, “What do I do with this? The neurotransmitter levels in the urine are already elevated”. The answer is, “Nothing, simply treat the patients like everyone else under the protocols”. Remember start up neurotransmitter testing is of no value and THIS IS the reason.

Considerations are as follows:

1. Cross checking urinary neurotransmitter testing with salivary neurotransmitter testing (which is still experimental) shows that these patients have markedly elevated urinary neurotransmitter levels and very low salivary neurotransmitter levels
2. There appears to be an inappropriate excretion of neurotransmitters taking place whereby the kidney is hyperexcreting and in turn depleting.
3. The mechanism of action of this Hyperexcretion remains unknown.
4. Amino acid therapy corrects the problem and brings the system levels of neurotransmitters back to normal or therapeutic levels.

The full impact of hyperexcretion has appreciated, but it appears to have established itself as a major consideration in amino acid therapy and neurotransmitter dysfunction. The prototype disease here is attention deficit hyperactivity disorder (ADHD). While ADHD is primarily associated with children there is a growing awareness of it in adults. A prominent psychiatrist in our area recently made the comment, “Only about 3 to 4% of adults with ADHD are being diagnosed.”

Decrease in systemic neurotransmitter levels correlates directly with diminished cognitive function. The other side of the coin is that as urinary neurotransmitter levels increase above the high end of normal there is an inverse correlation with cognitive function. An interesting article that was sent to me recently in which the researchers had come to the conclusion that patients with increased levels of neurotransmitters in the urine correlated inversely with IQ, i.e. as the urinary neurotransmitter levels increase in patients not under treatment with amino acids there was an associated decrease in IQ.

There indeed is a strong correlation between increased urinary neurotransmitter levels and ADHD in both children and adults. In general in the elderly population there is an increase in hyperexcretion of neurotransmitters. No studies have been done as of yet on the effects of addressing hyperexcretion of neurotransmitters and its impact on cognitive decline in the elderly.

Neurotransmitter testing for hyperexcretion of neurotransmitters is a viable option to verify the etiology of a suspected problem, but the proper groundwork has not been done with clinical observations and work. An empirical trial with amino acids and close observation without testing may be just as acceptable.