

**NEUROSCIENCE**



Professional Series

# Autism and Neurotoxins



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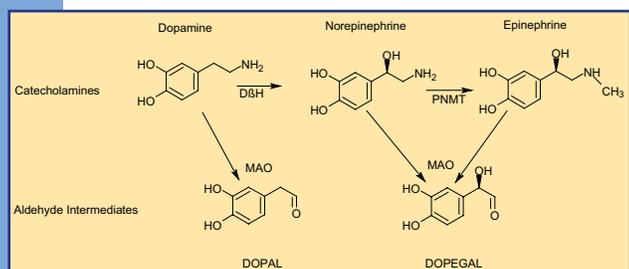
BETTER HEALTH THROUGH BETTER SCIENCE

## Background

Autism is characterized by a spectrum of behaviors and developmental delays that are generally attributed to a complex set of neurological disturbances that result from a combination of genetic and environmental factors. Many of the alternative treatment approaches or adjunct therapies for patients with neurodegenerative disorders are designed to improve methylation and detoxification pathways. These treatments generally view the environment or other external sources, like mercury in vaccines, as the origin of the neurotoxic substances. Neurotoxins are defined as chemical substances that are lethal to neurons. While the environment certainly can be a source of neurotoxins, these therapeutic protocols overlook the fact that neurotoxic substances may originate within the body and can actually be formed within the neurons themselves.

## Neurotoxin Synthesis

Neurotransmitters are metabolized in a two-step process that utilizes the enzymes monoamine oxidase (MAO) and aldehyde dehydrogenase. The first step involves MAO, which is present within the cytoplasm of neurons, and breaks down neurotransmitters to form highly reactive aldehyde intermediates. The dopamine metabolite DOPAL (3-, 4-dihydroxyphenylethanol) is one of the reactive aldehyde intermediates formed by MAO and is a potent neurotoxin. Studies have found that Parkinson's-like brain lesions can be induced with DOPAL and that the cognitive impairment seen has similarities to autism<sup>1</sup>.



**Figure 1** Catecholamine metabolism pathway including the formation of the neurotoxic aldehyde intermediates, DOPAL and DOPEGAL. Adopted from Eisenhofer, et al.

MAO is a mitochondrial enzyme and is present inside the neurons, but not inside the neurotransmitter vesicles within the neuron. As such, DOPAL and related reactive neurotransmitter aldehydes are formed from neurotransmitter pools that are present inside a neuron, but outside of the intracellular vesicles. Excessive catecholamine (dopamine, norepinephrine, and epinephrine) neurotransmitter turnover, the sum of neurotransmitter firing and reuptake, increases

the production of these neurotoxins. In order to limit the formation of these aldehydes, it is necessary to limit the supply of neurotransmitters present in the cytoplasm.

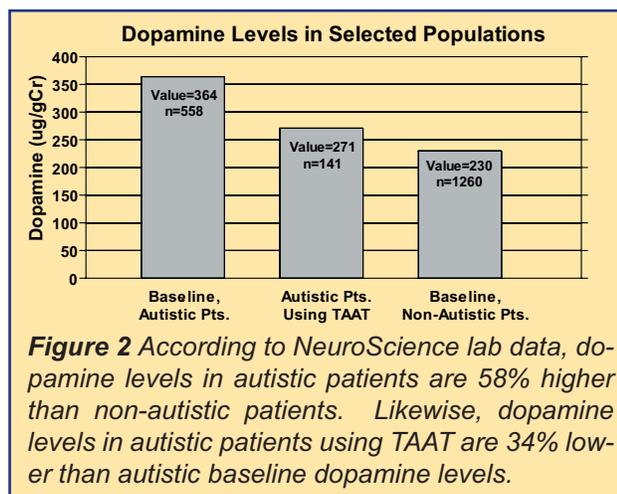
A common misconception regarding neurotransmitter turnover and degradation is that neurotransmitter molecules are only released from the vesicles via synaptic release and that the neurotransmitters degraded by MAO are only those that have been returned to the neuron through an active reuptake mechanism. While it is true that this is one source of neurotransmitter degradation products, neurotransmitters can also leak out of vesicles directly. This leaking process is a significant source of neurotransmitters degraded by MAO and therefore neurotoxin formation. In summary, neurotoxic aldehyde formation comes from two sources:

- reuptake degradation
- vesicle leakage degradation

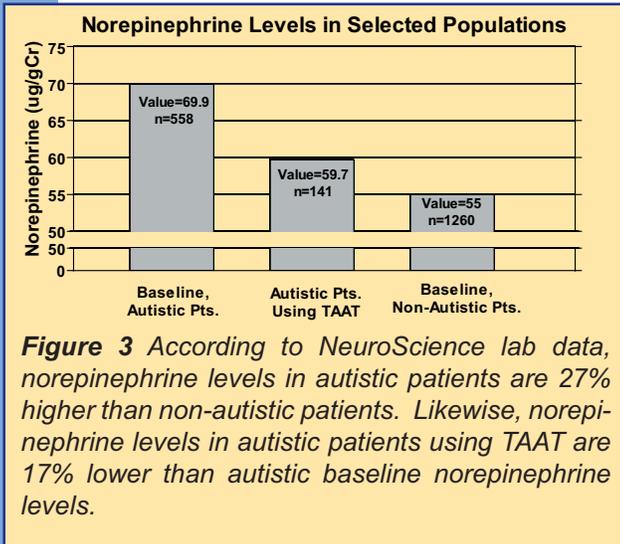
In a normal healthy situation, the active release of neurotransmitters and subsequent reuptake contributes only a very small fraction <2% of the neurotransmitters metabolized by MAO to form the neurotoxic reactive aldehydes. The primary source >98% is the constant non-specific leaking of neurotransmitters directly from the vesicles. This situation changes dramatically when neurons are highly stimulated. In this situation >60% of the neurotransmitters susceptible to MAO degradation and aldehyde formation originate from the active release and reuptake of neurotransmitters and <40% are from the non-specific leaking of vesicles. This high rate of firing can be pathogenic because it significantly increases the formation of toxic metabolites within the neuron and increases the risk of neurological damage.

## Neurotoxins & Autism

Many patients with autism have high urinary levels



**Figure 2** According to Neuroscience lab data, dopamine levels in autistic patients are 58% higher than non-autistic patients. Likewise, dopamine levels in autistic patients using TAAT are 34% lower than autistic baseline dopamine levels.



**Figure 3** According to NeuroScience lab data, norepinephrine levels in autistic patients are 27% higher than non-autistic patients. Likewise, norepinephrine levels in autistic patients using TAAT are 17% lower than autistic baseline norepinephrine levels.

of neurotransmitters indicating an increased rate of neurotransmitter turnover. Insufficient regulation of excitatory neurotransmitters increases the high rate of neurotransmitter release and reuptake and increases neurotransmitter exposure to MAO. Unchecked, excitatory neurotransmitters will cause rapid and repeated neuron firing and increase neurotoxin formation<sup>2</sup>. Interventions that reduce high rates of neurotransmitter turnover will also reduce the formation of toxic aldehydes and as a consequence can reduce neurological damage.

Raising the level of inhibitory neurotransmitters will decrease the rate of firing and decrease aldehyde formation. Because over-stimulation results in the formation of toxic compounds and neurological damage, it may also contribute to the development of symptoms seen in autistic patients. Urinary testing of neurotransmitter levels confirms that supporting the inhibitory neurotransmitters with Targeted Amino Acid Therapy (TAAT) will reduce the excretion of excitatory neurotransmitters.

## Case Study:Autism & TAAT

- **Patient:** M
- **DOB:** 9/21/00
- **History:** Diagnosed Autistic with significant hand flapping and low social interaction
- **Medications:** None

### Introduction:

The patient's mother was searching for a treatment program that would decrease or eliminate her son's hand-flapping, a common symptom in autistic patients. The mother also was hoping to develop her son's social skills, particularly his ability to communicate verbally. The doctor ordered a urine test to identify neurotransmitter imbalances.

	Optimal Range	Baseline Test	1 <sup>st</sup> Retest	2 <sup>nd</sup> Retest
Epinephrine	8-12	<b>22.8</b>		
Norepinephrine	30-55	<b>61.3</b>		
Dopamine	125-175	<b>346.8</b>		
Serotonin	175-225	<b>107.2</b>		
GABA	2.0-4.0	<b>12.1</b>		
Glutamate	10-25	<b>49.2</b>		
PEA	175-350	<b>789</b>		
Histamine	10-22	<b>35.1</b>		

### Comment:

The baseline neurotransmitter test indicated significant elevations in each of the catecholamine levels, as well as the excitatory neurotransmitters glutamate, PEA, and histamine. Serotonin was found to be quite low. The Doctor initiated a TAAT program designed to elevate serotonin and decrease the level of excitatory transmitters. The goal of the program was to provide symptomatic relief in addition to preventing further neurotoxic damage from the reactive aldehydes.

	Optimal Range	Baseline Test	1 <sup>st</sup> Retest	2 <sup>nd</sup> Retest
Epinephrine	8-12	22.8	<b>19.4</b>	
Norepinephrine	30-55	61.3	<b>55.9</b>	
Dopamine	125-175	346.8	<b>160.2</b>	
Serotonin	175-225	107.2	<b>190.3</b>	
GABA	2.0-4.0	12.1	<b>9.9</b>	
Glutamate	10-25	49.2	<b>29.5</b>	
PEA	175-350	789	<b>652</b>	
Histamine	10-22	35.1	<b>27.4</b>	

### Comment:

After 2 months of treatment another urine test was performed. The test showed dramatic improvements in the patient's neurotransmitter profile, most notably the catecholamines. The patient's mother reported some improvement in the child's behavior. The incidence of hand flapping had decreased and the child was slightly more social. The doctor suggested the patient remain on the therapeutic protocol.

	Optimal Range	Baseline Test	1 <sup>st</sup> Retest	2 <sup>nd</sup> Retest
Epinephrine	8-12	22.8	19.4	<b>9.6</b>
Norepinephrine	30-55	61.3	55.9	<b>47.5</b>
Dopamine	125-175	346.8	160.2	<b>168.0</b>
Serotonin	175-225	107.2	190.3	<b>458.3</b>
GABA	2.0-4.0	12.1	9.9	<b>8.0</b>
Glutamate	10-25	49.2	29.5	<b>27.3</b>
PEA	175-350	789	652	<b>618</b>
Histamine	10-22	35.1	27.4	<b>20.8</b>

## Comment:

After an additional 2 months of treatment, another urine sample was collected. The test showed continued improvements in the patient's neurotransmitter profile. The patient's mother reported that the flapping had almost ceased, only noting a couple of episodes in the past month. The patient's verbal skills had also improved steadily. Satisfied with the progress made thus far, the doctor recommended continuing the therapy at maintenance-level doses with periodic retesting to monitor neurotransmitter levels.

## Summary:

Many autistic patients have elevated urinary catecholamine (dopamine, norepinephrine, and epinephrine) levels, indicating a high rate of neurotransmitter turnover. Supporting inhibitory neurotransmitters with a TAAT program has been shown to decrease urinary levels of catecholamines and therefore is a method to decrease the rate of catecholamine turnover. TAAT can be used to decrease the rate of neurotoxic aldehyde formation by MAO, and reduce the risk of further neurological damage in patients with autism.

## References:

1. Burke WJ, Li SW, Williams EA, Nonneman R, Zahm DS. *3,4-Dihydroxyphenylacetaldehyde is the toxic dopamine metabolite in vivo: implications for Parkinson's disease pathogenesis. Brain Res. 2003 Nov 7;989(2):205-13.*
2. Eisenhofer G, Kopin IJ, Goldstein DS. *Leaky catecholamine stores: undue waste or a stress response coping mechanism? Ann N Y Acad Sci. 2004 Jun;1018:224-30.*

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