# Neurotrophic Hormone Deficiency Theory

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## Table of contents



## 1 Overview

Neurotrophic Hormone Deficiency Theory was originally proposed by Appel et al., (1981) and is a theory for a common underlying cause of ALS, Parkinsonism, and Alzheimer's Disease.

## 2 Commonalities of ALS, PD, and AD

To understand this theory, one must first understand the overlapping concepts of each of these diseases.

- All 3 diseases have changes in presynpatic neuronal input with secondary alterations of the target tissue[1]
- All 3 diseases sporadically occur later in life and the incidence increases with age[1]
- All 3 diseases have a familial form that occurs in 5-10% of patients[1]
- Heavy metal intoxication is a secondary cause of these diseases[1]

### 2.1 Presynaptic neuron changes + Target tissue alterations

- ALS has changes in Betz cells, CN motor neurons, and anterior horn cells[1]
- PD includes changes in Substantia nigra neurons[1]
- Alzheimer's disease includes changes in the cholinergic input from nucleus basalis and septal neurons to cortex and hippocampus[1]

### 2.2 Secondary Heavy Metal Onset

- ALS: Lead[1]
- PD: Manganese[1]
- Alzheimer's Disease: Aluminum (evidence is weak)[1]

## 3 Accelerated Aging Theory

plays into the theory that the relevant neural areas are experiencing accelerated aging, and therefore and degenerating faster[1]. Neurotrophic Hormone Deficiency Theory adds to the accelerated aging idea by suggesting that the areas that undergo accelerated aging is based on intrinsic neuronal properties[1].

## Advantages of the theory

1. This theory explains why external causes such as viral nor abnormal factors have yet to be discovered for these 3 diseases.
2. This theory helps to explain why there is a prevailing and consistent genetic incidence of ALS, PD, AD[1]
3. Accelerated aging explains why disease incidence worsens with age[1]
4. Lastly, this theory explains why external toxic factors such as heavy metal toxicity, trauma, viruses, infections, and vascular disease may increase the progression of these diseases

### 3.1 Disadvantages

- It should be noted that this theory does not provide specific insight as to the selective vulnerability of these neuronal networks[1].
- This theory does not offer meaningful and potentially useful therapeutic approahes to ALS, PD, or dementia/AD[1].

1. Appel SH. A unifying hypothesis for the cause of amyotrophic lateral sclerosis, parkinsonism, and Alzheimer disease. *Annals of Neurology*. 1981;10(6):499-505. doi:10.1002/ana.410100602