



# Dissolving the Plaque Trehalose: A Novel Treatment

Dr. Jared M. Skowron, ND  
Amazon Best-Selling Author

**100**  
**NATURAL  
REMEDIES  
FOR YOUR  
CHILD**

THE COMPLETE GUIDE TO  
Safe, Effective Treatments  
for Childhood's Most  
Common Ailments,  
from ALLERGIES  
to WEIGHT LOSS



Dr. Jared Skowron



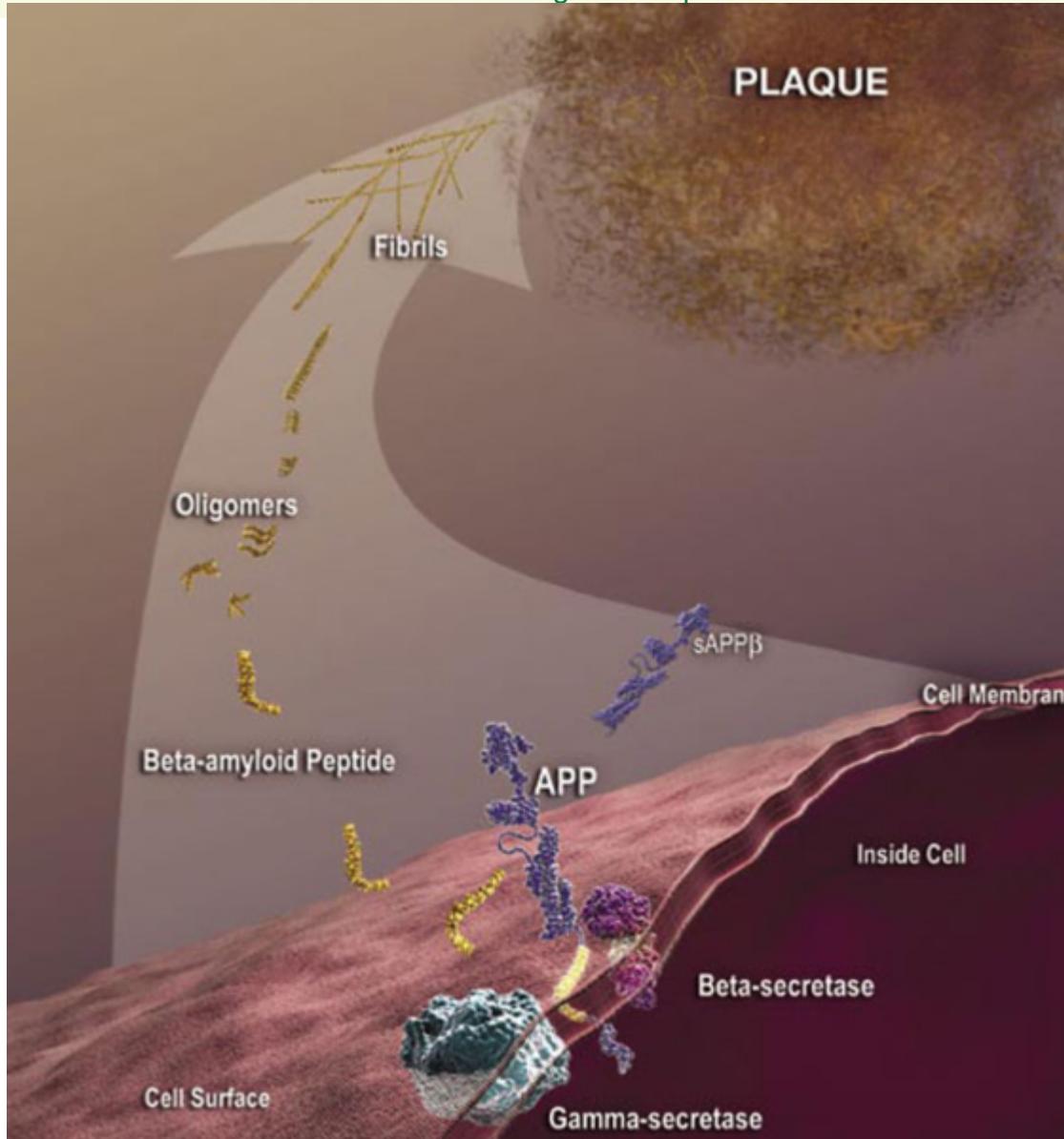
AUTISM HOPE



ALLIANCE



**Spectrum Awakening**



# Down & Amyloid

- Amyloid Precursor Proteins
- Increased in Down and Alzheimer and Autism
- Perturbs axonal pathfinding and circuit formation
- Neurobiol Aging. 2014 May;35(5):958-68. doi: 10.1016/j.neurobiolaging.2013.08.039.
- FASEB J. 2014 Jan;28(1):195-205. doi: 10.1096/fj.13-232686.
- J Neuroinflammation. 2013 Jul 16;10:84. doi: 10.1186/1742-2094-10-84.



# Down & Amyloid

- Over-production of amyloid beta peptides plays the dominant role of dementia
- Adults with Down that reach the age of 40 have neuropathology to match Alzheimer diagnosis

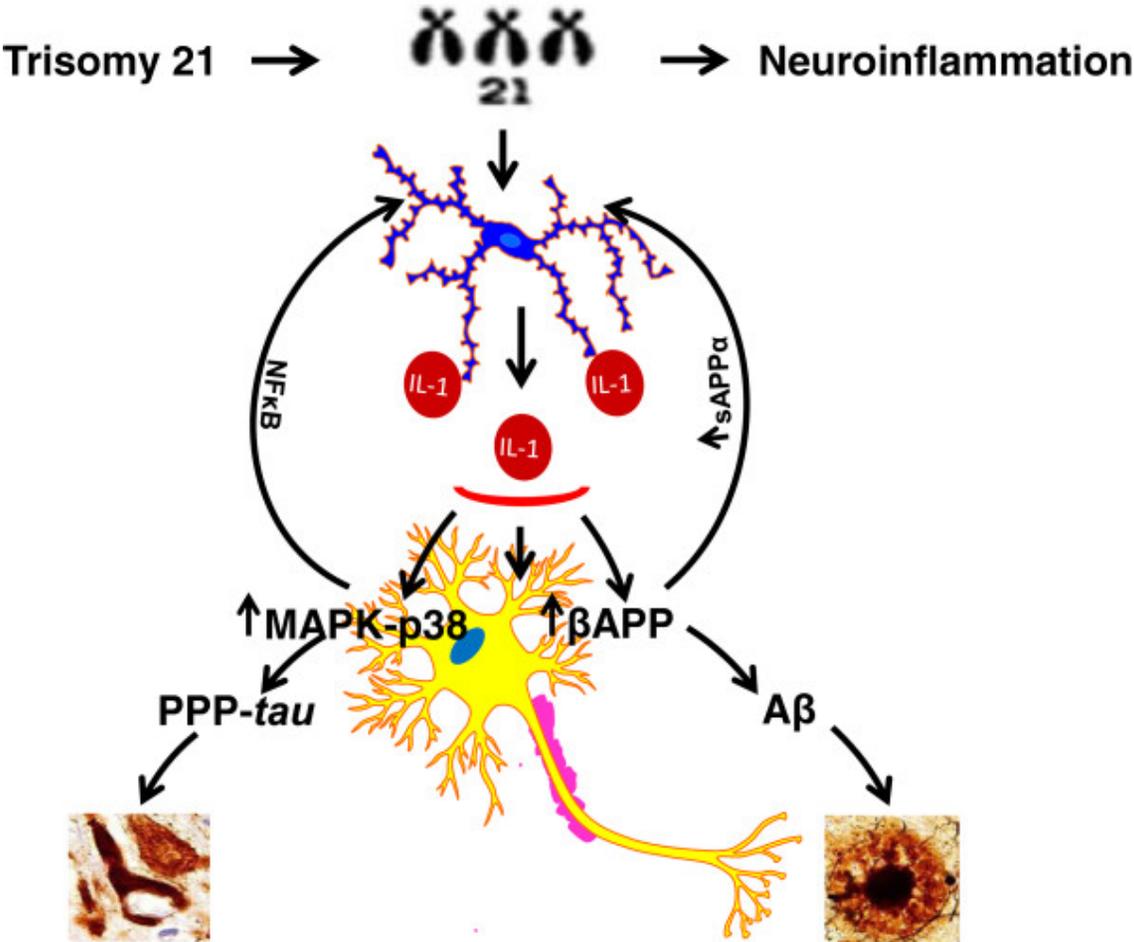
- [Autoimmun Rev.](#) 2013 Apr;12(6):670-3. doi: 10.1016/j.autrev.2012.10.013.
- [Alzheimers Dement.](#) 2012 Nov;8(6):496-501. doi: 10.1016/j.jalz.2011.09.229.
- [Prog Brain Res.](#) 2012;197:101-21. doi: 10.1016/B978-0-444-54299-1.00006-6.
- [Biochim Biophys Acta.](#) 2012 Feb;1822(2):130-8. doi: 10.1016/j.bbadis.2011.10.001.

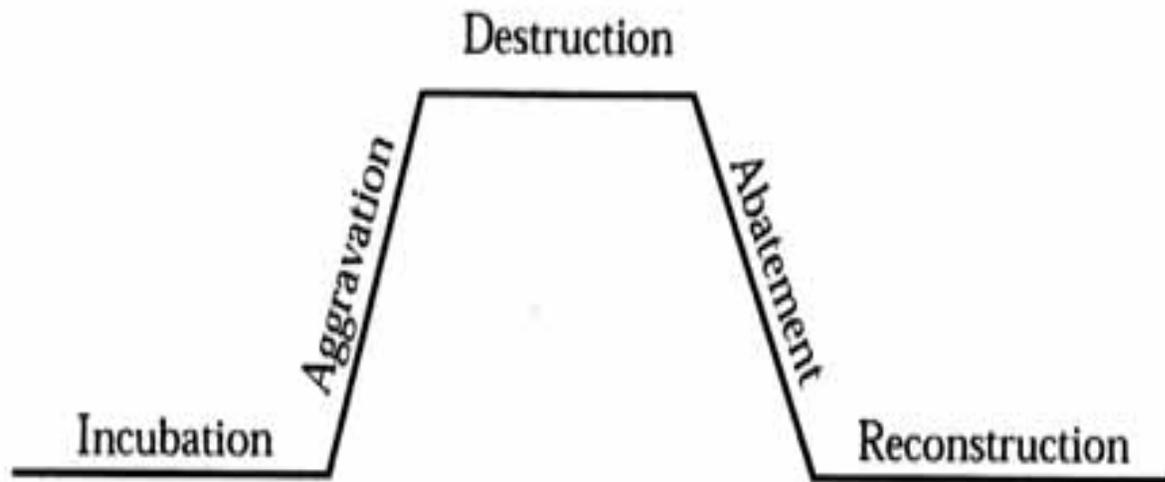


# Order of Disease

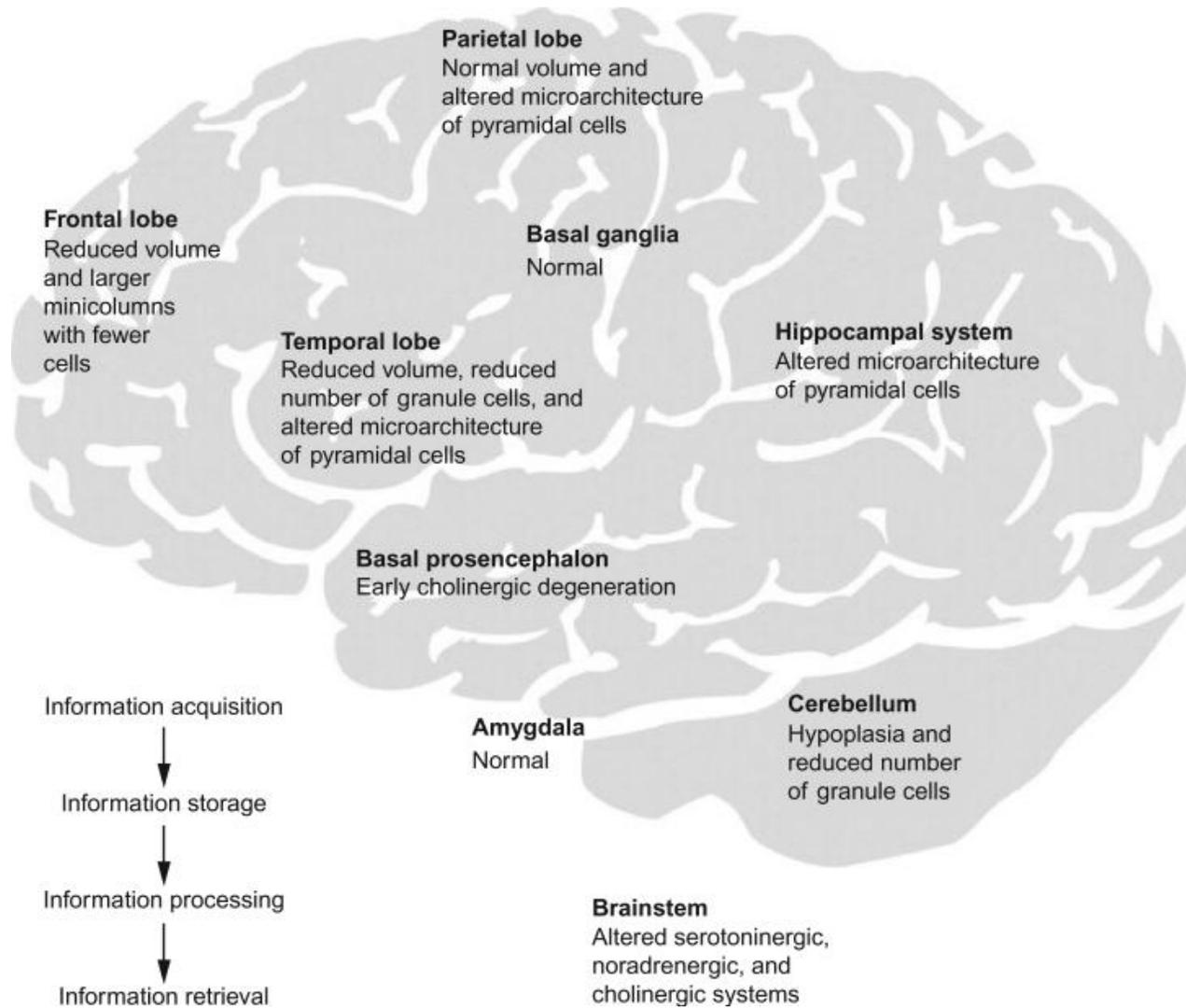
- Symptom Presentation
  - Physiological creation of symptoms
  - Homeostatis (inflammation)
  - Etiological stressor
- ↑
- ↑
- ↑



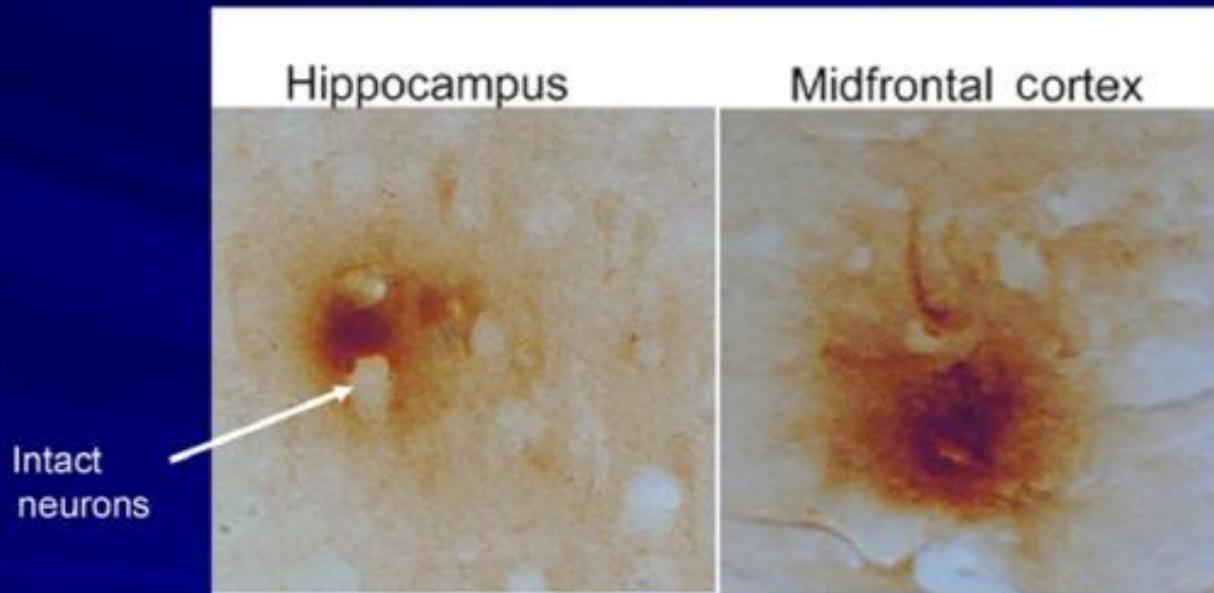




Dissolving the Plaque: Trehalose - Dr. Jared M. Skowron, ND

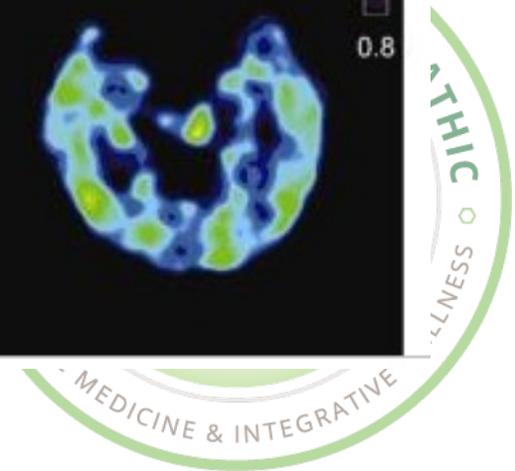
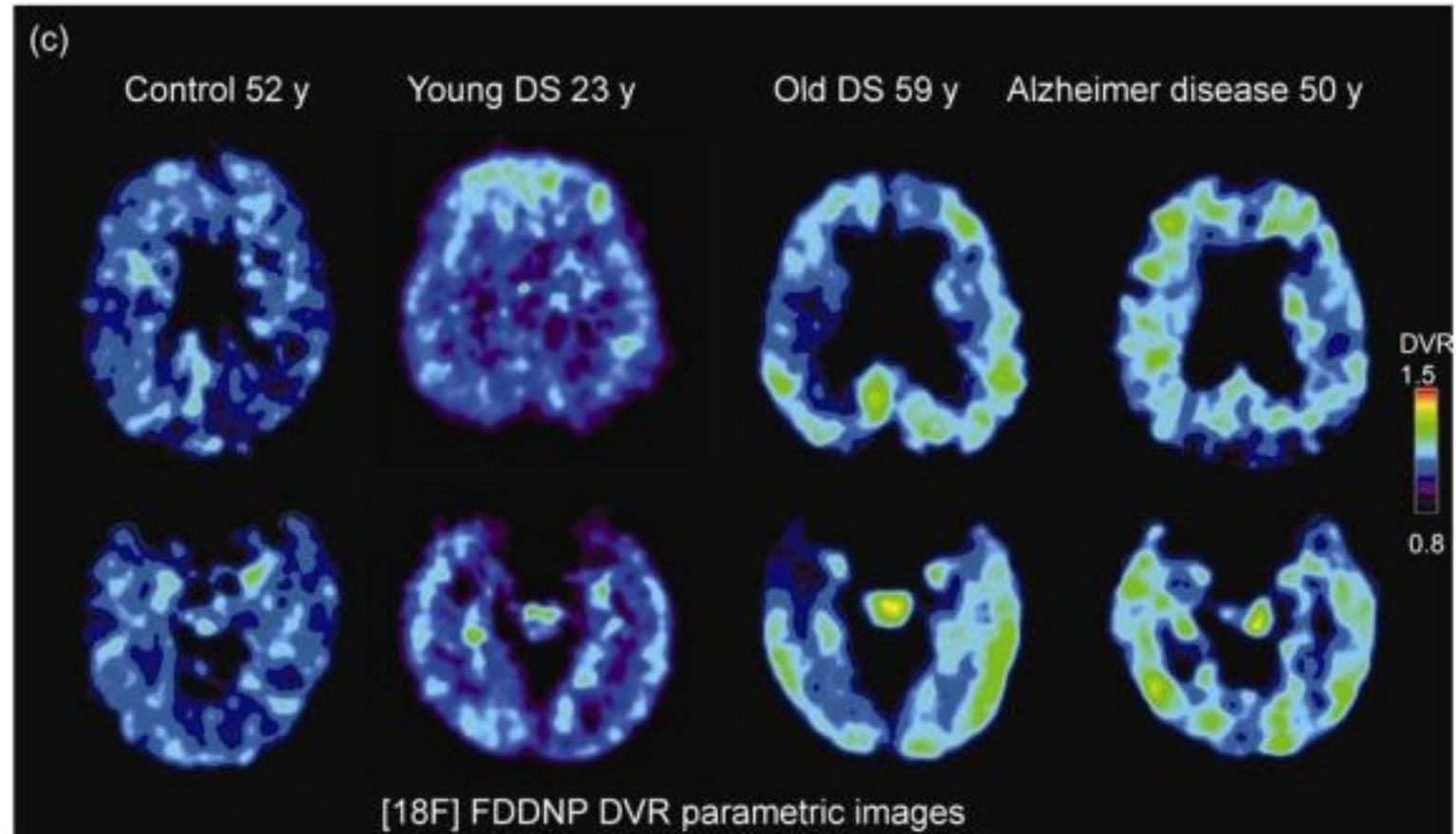


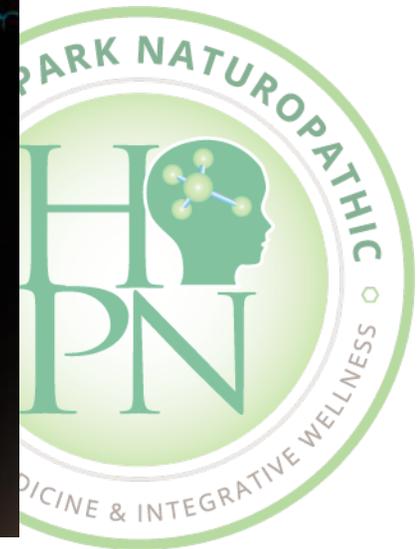
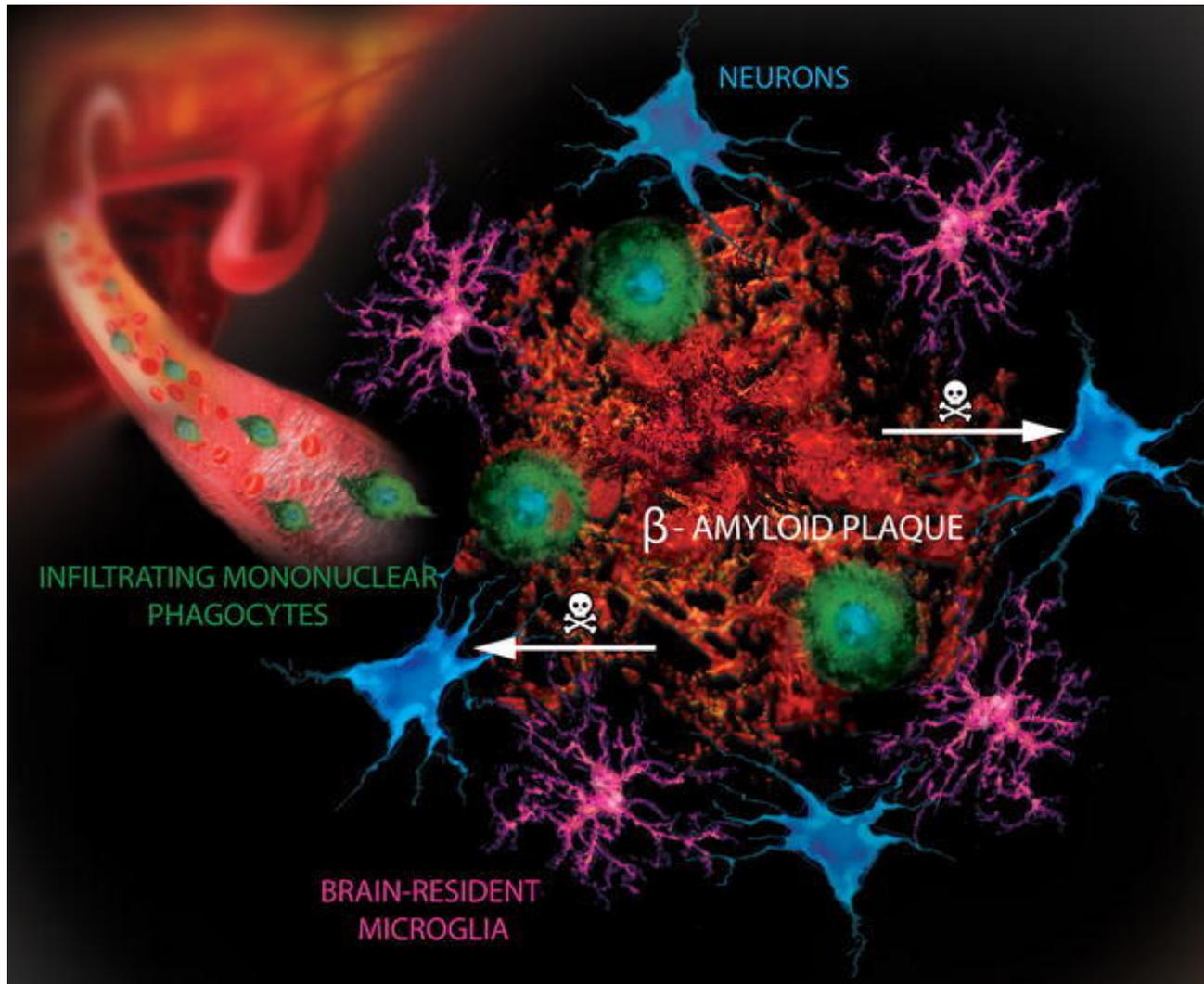
## Early onset A $\beta$ in Down syndrome



4 months old – anti-A $\beta$ 1-16 immunostaining in free-floating formic acid pretreated 50  $\mu$ m thick formalin-fixed sections.







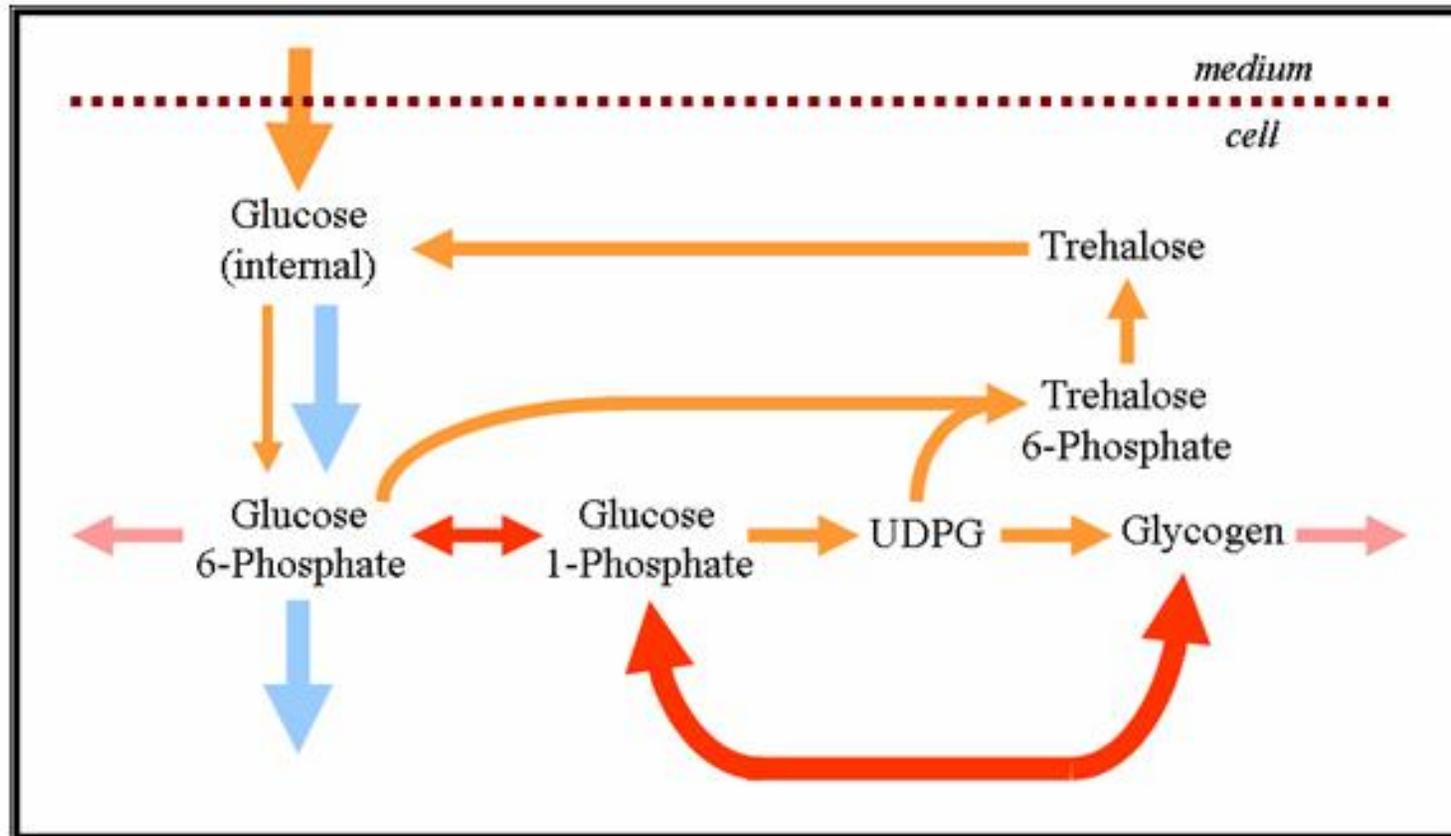


# The Callous On My Foot

# Brain Plaques

- Plaque development is the result of prolonged inflammation
  - Worsens neurological function
- Trehalose is a potential treatment
  - Remove the plaques
  - Currently in Alzheimer's research





Genes involved in the trehalose cycle and degrees of their up-regulation 10 – 20 minutes after moderate heat shock (37° C). Thickness of red, orange and pink arrows indicates the magnitude of up-regulation. Blue arrows indicate that these steps are unaltered over baseline.



# Brain Plaques

- Down, Alzheimer, & Autism are linked with presence of amyloid material in the brain
  - sAPP-alpha
    - 60% severely autistic children
    - Immune dysfunction
    - Brain overgrowth – 90%
  - Amyloid-beta17-40 and Amyloid-beta17-42
    - Neurotoxic
    - Stimulates aggregation
    - Deposition of Alzheimer-type beta-amyloid plaques
    - Cause astrocyte proliferation – risk for plaques



# Amyloid Material

- sAPP-alpha elevation
  - Response to brain injury
  - Glutamate toxicity
  - Excess IL-6 and NF-kB
  - Toxic exposure
  - Nutritional deficiencies
- Amyloid-beta17-40, 17-42 elevation
  - Attracted to astrocytes
  - Attracted to lipofuscin



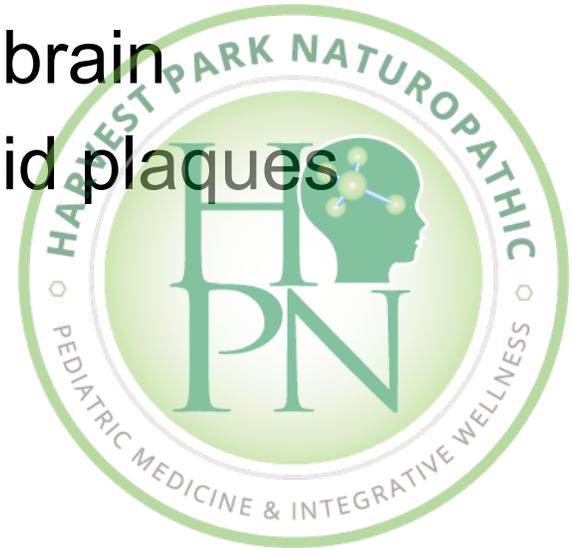
# Amyloid Plaques

- Accumulation of amyloid material in childhood increases risk of amyloid plaque formation
- Down children probably have current amyloid plaque formation
- Beta-Amyloid plaques
  - Neuron cell death
  - Impairs synaptic transmission
  - Impairs neurotransmitter release
  - Enhances myelin lipid peroxidation
  - Enhances NMDA-induced excitotoxicity
  - Creates free radicals and pro-inflammatory cytokines



# Treatment Goals

- Reduce aggregation of plaque-forming amyloid material
- Reduce neurotoxicity
- Reduce oxidative stress in the brain
- Prevent the formation of amyloid plaques



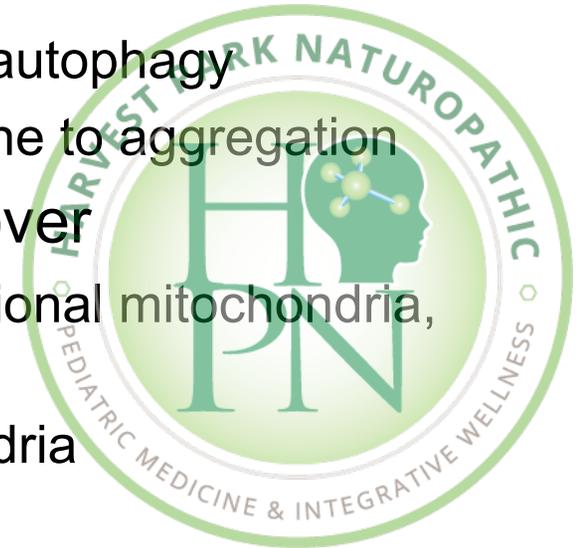
# Trehalose

- Disaccharide composed of two glucose molecules linked through glycosidic bond
- Shown to be absorbed and cross BBB in mice
  - Stabilize protein structure as a molecular chaperone
  - Inhibits amyloid aggregation in vitro
  - Dissolves pre-formed amyloid aggregates
  - Protects neural cells from amyloid aggregates
  - Reduces neurotoxicity
  - Creates healthy mitochondrial function



# mTOR-independent autophagy enhancer

- Bulk degradation of unwanted cellular material
  - Amyloid aggregates phagocytosis and lysosome destruction
- Trehalose upregulates autophagic removal of amyloid material
  - Beta-amyloid material shown to inhibit autophagy
  - Special affinity for proteins that are prone to aggregation
- Trehalose promotes organelle turnover
  - Protects from accumulation of dysfunctional mitochondria, acts as an anti-oxidant
  - Promote formation of healthy mitochondria

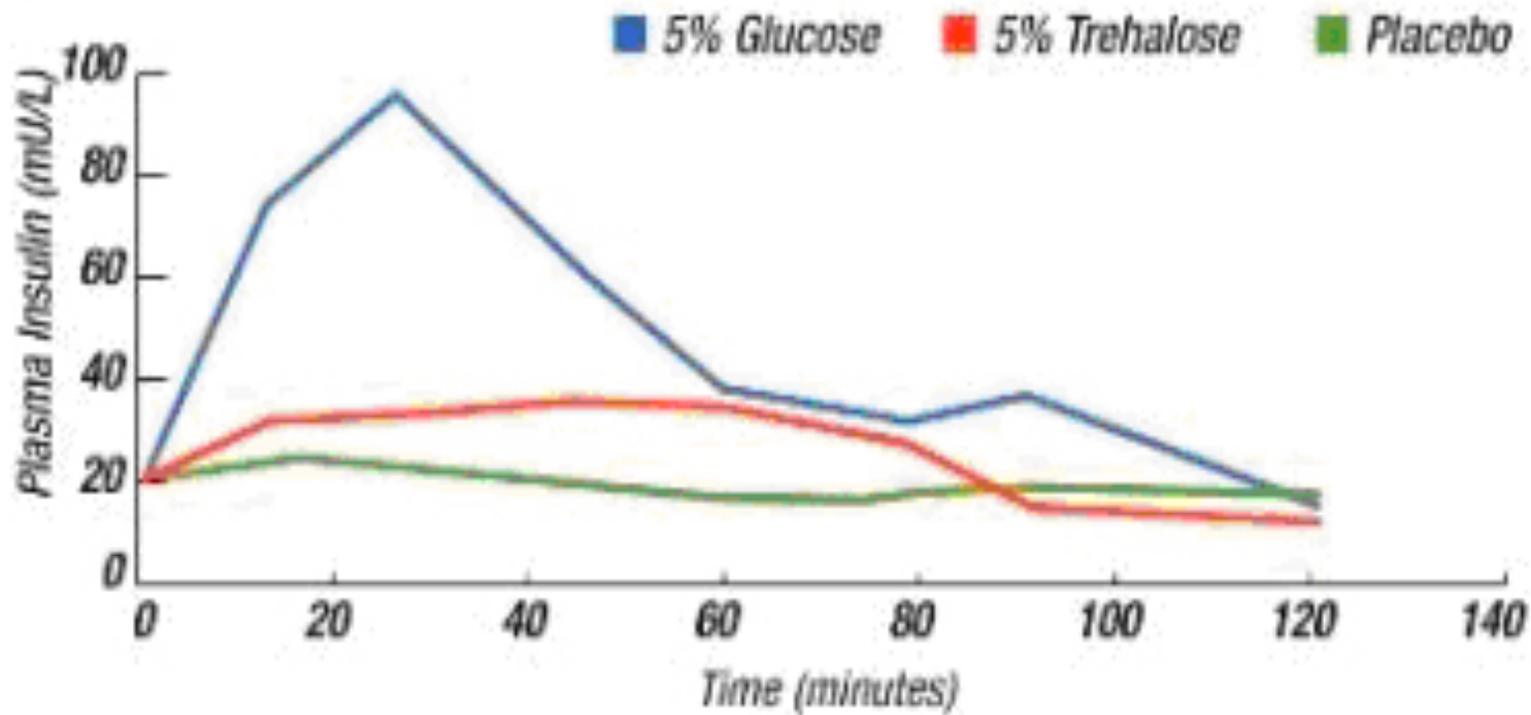


# Trehalose Safety

- US FDA gives Trehalose a GRAS rating
  - Generally regarded as safe
- Safe in doses as high as 50g per day
- May lead to minor gastrointestinal upset
  - 15% lack Trehalase enzyme



### Plasma insulin levels after consumption of beverages



# Trehalose Pilot Study

- Open-label, 45 days
- Before and after ATEC survey
  - Autism Treatment Evaluation Checklist
- 12 children enrolled
  - 5 dropped out due to GI distress



# Trehalose Study Results

- Language - 10% improvement
  - Normal conversation, communication
  - More words per sentence
- Sociability - 14% improvement
  - Eye contact, cooperative
  - Command compliance, fewer tantrums
- Cognition - 12% improvement
  - Aware of others, curious of environment
- General Health - 12% improvement
  - Happier, less OCD, less agitated
  - Better toilet training

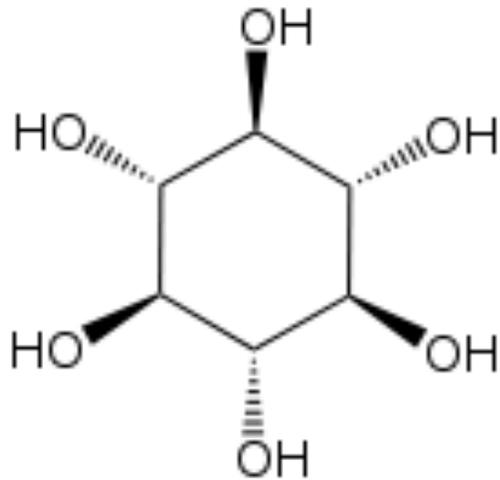


# Inositol Treatment

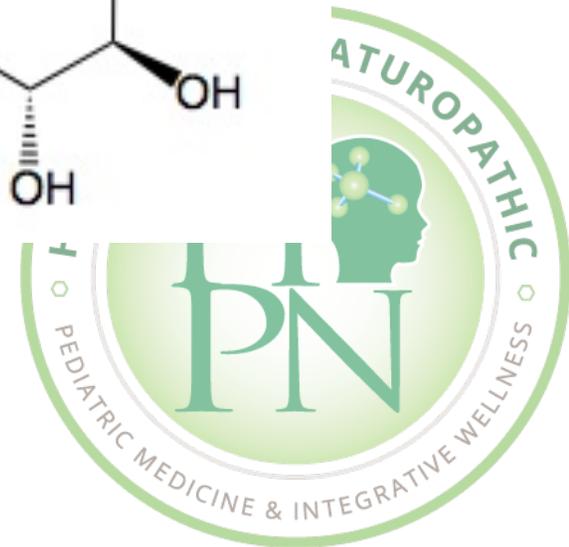
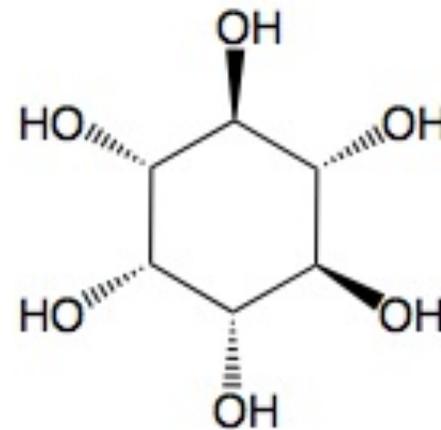
- Scyllo-inositol
  - Another treatment to prevent plaque accumulation
  - Currently in Alzheimer research
- Also inhibits amyloid plaque growth
  - Binds pre-fibrillar aggregates
- Scyllo-inositol converted from myo-inositol with probiotics
- Found in purple yam, eggplant, artichoke, chicory, escarole, and endive
- [J Am Chem Soc.](#) 2013 Nov 13;135(45):16926-37. doi: 10.1021/ja406197f.
- [J Phys Chem B.](#) 2012 Jan 26;116(3):1111-9. doi: 10.1021/jp208567n.
- [Microb Cell Fact.](#) 2011 Sep 7;10:69. doi: 10.1186/1475-2859-10-69.



## Scyllo-Inositol



## Myo-Inositol



# Summary

- Dissolve the Plaque
- Inflammation is cause of chronic disease
  - Scar/Plaque is the reaction of chronic inflammation
- Amyloid plaque reduces brain function and memory
- Prevent and Dissolve the Plaque
- Treatment Summary
  - Super Trehalose 3,000 mg
  - Inositol 3,000 mg



# Research TGF

- <http://www.ncbi.nlm.nih.gov/pubmed/23363776> - Vitamin A, TGF
- <http://www.ncbi.nlm.nih.gov/pubmed/23132743> - VDR, TGF
- <http://www.ncbi.nlm.nih.gov/pubmed/19087699> - Vit D, TGF
- <http://www.ncbi.nlm.nih.gov/pubmed/12548714> - Vit D, anti-infl
- <http://www.ncbi.nlm.nih.gov/pubmed/8632765> - TGF, amyloid
- <http://www.ncbi.nlm.nih.gov/pubmed/?term=tgf+herb+brain> - Danshen, TGF

# Research MIF

- <http://www.ncbi.nlm.nih.gov/pubmed/22281490> - Vitamin E
- <http://www.ncbi.nlm.nih.gov/pubmed/10609875> - Vitamin E
- <http://www.ncbi.nlm.nih.gov/pubmed/9739171> - Vitamin E

# Research Ig

- <http://www.ncbi.nlm.nih.gov/pubmed/22739370> - Vitamin A
- <http://www.ncbi.nlm.nih.gov/pubmed/21224870> - Vitamin D
- <http://www.ncbi.nlm.nih.gov/pubmed/20495123> - Vitamin E
- <http://www.ncbi.nlm.nih.gov/pubmed/8374246> - Zinc
- <http://www.ncbi.nlm.nih.gov/pubmed/21619924> - Herb

# Research estrogen

- <http://www.ncbi.nlm.nih.gov/pubmed/21359227> - estrogen
- <http://www.ncbi.nlm.nih.gov/pubmed/22674640> - D2:D4

# Research ANA

- <http://www.ncbi.nlm.nih.gov/pubmed/21586442> - Vit D
- <http://www.ncbi.nlm.nih.gov/pubmed/21713097> - NAC
- <http://www.ncbi.nlm.nih.gov/pubmed/23436141>

# Research Vitamin E

- <http://www.ncbi.nlm.nih.gov/pubmed/23336971>
- <http://www.ncbi.nlm.nih.gov/pubmed/22898564>
- <http://www.ncbi.nlm.nih.gov/pubmed/19623831>

# References

- Wegiel J, Frackowiak J, Mazur-Kolecka B, Schanen CN, Cook EH, Sigman M, et al. Abnormal intracellular accumulation and extracellular Abeta deposition in idiopathic and Dup15q11.2-q13 Autism Spectrum Disorders. PLoS ONE 2012 May 2;7(5):1-17.
- Liu R, Barkhordarian H, Emadi S, Park CB, Sierks MR. Trehalose differentially inhibits aggregation and neurotoxicity of beta-amyloid 40 and 42. Neurobiol Dis 2005 Feb 7;20(1):74-81.
- Mucke L, Selkoe DJ. Neurotoxicity of amyloid-beta protein: synaptic and network dysfunction. Cold Spring Harb Perspect Med 2012 Jul;2(7):1-17.
- Al-Ayadhi LY, Bacha ABG, Kotb M, El-Ansary AK. A novel study on amyloid beta 40, 42 and 40/42 ratio in Saudi autistics. Behav Brain Funct 2012 Jan;13(8):1-8.
- Sarkar S, Davies JE, Huang Z, Tunnacliffe A, Rubinsztein DC. Trehalose, a novel mTOR independent autophagy enhancer, accelerates the clearance of mutant huntingtin and alpha synuclein. J Biol Chem 2007 Feb 23;282(8):5641-52.
- Sokol DK, Chen D, Farlow MR, Dunn DW, Maloney B, Zimmer JA, et al. High levels of Alzheimer's beta-amyloid precursor protein (APP) in children with severely autistic behavior and aggression. J Child Neurol 2006 Jun;21(6):444-9.
- Sokol DK, Maloney B, Long JM, Ray B, Lahiri DK. Autism, Alzheimer's Disease, and fragile X: APP, FMRP, and mGluR5 are molecular links. Neurology 2011 April 12;76(15):1344-52.
- Antoinette RB, Giunta BN, Obregon D, Nikolic WV, Tian J, Sanberg CD, et al. Peripheral biomarkers in autism: secreted amyloid precursor protein alpha as a probable key player in early diagnosis. Int J Clin Exp Med 2008;(1):338-44.

# References

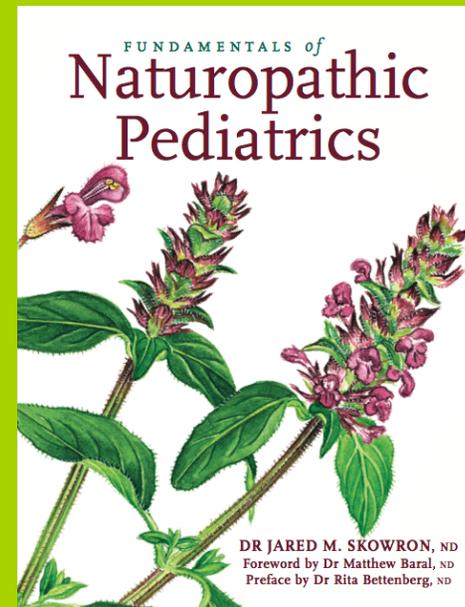
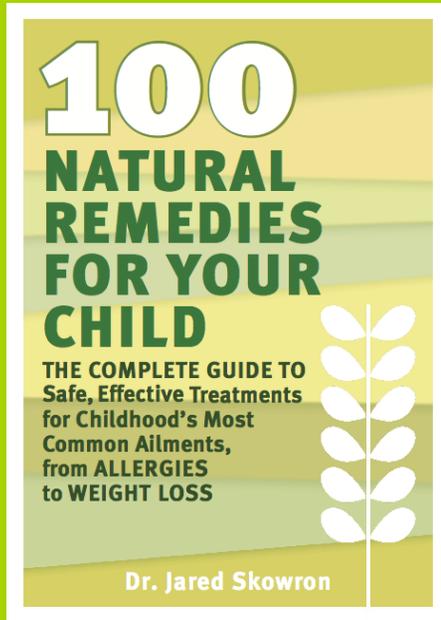
- Westmark CJ. What's hAPPening at the synapses? The role of amyloid-beta protein precursor and beta amyloid in neurologic disorders. *Mol Psychiatry*. forthcoming 2012.
- Bailey AR, Hou H, Obregon DH, Tian J, Zhu Y, Zou Q, et al. Aberrant T-lymphocyte development and function in mice overexpressing human soluble amyloid precursor protein alpha: implications for autism. *FASEB J* 2012 Mar;26(3):1040-51.
- Ray B, Long JM, Sokol DK, Lahiri DK. Increased secreted amyloid precursor protein alpha (sAPP-alpha) in severe autism: proposal of a specific, anabolic pathway and putative biomarker. *PLoS ONE* 2011 Jun 22;6(6):1-10.
- El-Ansary A, Al-Ayadhi L. Lipid mediators in plasma of autism spectrum disorders. *Lipids Health Dis* 2012 Nov 21;11(1):160.
- El-Ansary A, Al-Daihan S, Al-Dbass A, Al-Ayadhi L. Measurement of selected ions related to oxidative stress and energy metabolism in Saudi autistic children. *Clin Biochem* 2010 Jan;43(1-2):63-70.
- Kruger U, Wang Y, Kumar S, Mandelkow EM. Autophagic degradation of tau in primary neurons and its enhancement by trehalose. *Neurobiol Aging* 2012 Oct;33(10):2291-305.
- Liu FF, Ji L, Dong XY, Sun Y. Molecular insight into the inhibition effect of trehalose on the nucleation and elongation of amyloid beta-peptide oligomers. *J Phys Biochem* 2009 Aug 13;113(32):11320-9.
- Liu R, McAllister C, Lyubchenko Y, Sierks MR. Residues 17-20 and 30-35 of beta-amyloid play critical roles in aggregation. *J Neurosci Res* 2004 Jan 15;75(2):162-71.
- Metcalf DJ, Garcia-Arencibia M, Hochfeld WE, Rubinsztein DC. Autophagy and misfolded proteins in neurodegeneration. *Exp Neurol* 2012 Nov;238(1):22-8.

# References

- Nixon RA, Yang DS. Autophagy failure in Alzheimer's disease – locating the primary defect. *Neurobiol Dis* 2011 Jul;43(1):38-45.
- Boland B, Kumar A, Lee S, Platt FM, Wegiel J, Huang Yu W, et al. Autophagy induction and autophagosome clearance in neurons: relationship to autophagic pathology in Alzheimer's disease. *Neurobiol Dis* 2008 Jul 2;28(27):6926-37.
- Lafay-Chebassier C, Paccalin M, Page G, Barc-Pain S, Perault-Pochat MC, Gil R, et al. mTOR/p70S6K signaling alteration by Amyloid-beta exposure as well as in APP-PS1 transgenic models and in patients with Alzheimer's disease. *J Neurochem* 2005;(94):215-25.
- Aguib Y, Heiseke A, Gilch S, Riemer C, Baier M, Schatzl HM, et al. Autophagic induction by trehalose counteracts cellular prion infection. *Autophagy* 2009 Apr;5(3):361-9
- Hof PR, Knabe R, Bovier P, Bouras C. Neuropathological observations in a case of autism presenting with self-injury behavior. *Acta Neuropathol* 1991;82(4):321-6.
- Marazziti D, Baroni S, Picchetti M, Landi P, Silvestri S, Vatteroni E, et al. Psychiatric disorders and mitochondrial dysfunction. *Eur Rev Med Pharmacol Sci* 2012 Feb;16(2):270-5.
- Richards AB, Krakowka S, Dexter LB, Schmid H, Wolterbeek AP, Kurimoto M, et al. Trehalose: a review of properties, history of use and human tolerance, and results of multiple safety studies. *Food Chem Toxicol* 2002 Jul;40(7):871-98.
- Bar A. Trehalose: produced by a novel enzymatic process. *Bioresearch Mangement and Consulting Ltd* 2000 May 8:1-105.
- Garbern JY, Neumann M, Trojanowski JQ, Lee VM, Feldman G, Norris JW, et al. A mutation affecting the sodium/proton exchanger, SLC9A6, causes mental retardation with tau deposition. *Brain* 2010 May;133(Pt 5):1391-402.

# References

- [Majewska MD](#), [Hill M](#), [Urbanowicz E](#), et al. Marked elevation of adrenal steroids, especially androgens, in saliva of prepubertal autistic children. *Eur Child Adolesc Psychiatry*. 2013 Sep 17.
- [Lakshmi Priya MD](#), [Geetha A](#), [Suganya V](#), et al. Abnormal circadian rhythm and cortisol excretion in autistic children: a clinical study. *Croat Med J*. 2013 Feb;54(1):33-41.
- [Corbett BA](#), [Schupp CW](#), [Lanni KE](#). Comparing biobehavioral profiles across two social stress paradigms in children with and without autism spectrum disorders. *Mol Autism*. 2012 Nov 17;3(1):13. doi: 10.1186/2040-2392-3-13.
- [Anderson CJ](#), [Colombo J](#), [Unruh KE](#). Pupil and salivary indicators of autonomic dysfunction in autism spectrum disorder. *Dev Psychobiol*. 2013 Jul;55(5):465-82. doi: 10.1002/dev.21051.
- [Putnam SK](#), [Lopata C](#), [Fox JD](#), et al. Comparison of saliva collection methods in children with high-functioning autism spectrum disorders: acceptability and recovery of cortisol. *Child Psychiatry Hum Dev*. 2012 Aug;43(4):560-73. doi: 10.1007/s10578-012-0284-3.
- [Iwata K](#), [Matsuzaki H](#), [Miyachi T](#), et al. Investigation of the serum levels of anterior pituitary hormones in male children with autism. *Mol Autism*. 2011 Oct 19;2:16. doi: 10.1186/2040-2392-2-16.
- [Rom 堯 GC](#), [Ghassabian A](#), [Bongers-Schokking JJ](#), et al. Association of gestational maternal hypothyroxinemia and increased autism risk. *Ann Neurol*. 2013 Aug 13. doi: 10.1002/ana.23976.
- [Hoshiko S](#), [Grether JK](#), [Windham GC](#), et al. Are thyroid hormone concentrations at birth associated with subsequent autism diagnosis? *Autism Res*. 2011 Dec;4(6):456-63. doi: 10.1002/aur.219.



Jared M. Skowron, ND

[www.SpectrumAwakening.com](http://www.SpectrumAwakening.com)

[www.NaturopathicAnswer.com](http://www.NaturopathicAnswer.com)