Lowering the risk for Alzheimer’s Disease

Intake: Nutrition & AD

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The Hippocampus

Hippocampal & cortical brain regions are affected in AD.
Neurons lose connections (synapses) Branches (dendrites) & eventually die in AD

Other cells involved include astrocytes, oligodendrocytes, microglia, & endothelia.
AD brain tissue has Aβ plaques & neurofibrillary tangles of p-tau
In a “library” of compounds we discovered “DDL110”, an sAPPα-enhancer. It is now in clinical trials for Mild Cognitive Impairment & AD.
Early diagnosis & treatment with more than one drug. Drugs are more likely to work if overall health is improved.

Multimodal treatment

Early & accurate diagnosis

Combination drug therapy

Healthstyle support

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Intake
Scientific/biochemical bases for effects of nutrition & medication are discussed.

Output
Interactions, intellectual challenges, exercise, stress reduction & sleep are discussed.
Healthy food
Anti-oxidant rich
Low sugar
Fewer calories
Reduce gluten
Lower protein
A little caffeine (if tolerated)
A little red wine (not if an alcohol problem is present)
Probiotics
Folic acid, B6, B12, D3
Mitochondria (powerhouses of the cell) use $O_2$ ($O:O$) generating radicals ($O.$) missing an electron. Radicals will steal electrons from DNA & proteins, damaging tissue. Anti-oxidants are “radical scavengers” with electrons to donate.
High energy use generates radicals. Damage accumulates in long-lived neurons.

Positron Emission Tomography (PET) shows low glucose utilization in AD brain due to damage.

Anti-oxidants may prevent this damage.
Anti-oxidants: A Rainbow of Possibilities

Vitamin C & E in food best, excesses may not be of benefit
- Turmeric (curcumin)
- Blueberry (tocopherols)
- Apples (quercetin, catechin)
- Avocado (lutein)
- Cabbage (anthocyanin)
- Green tea (flavonoids)
Indian, Greek, Italian!

Cook to have control over your food
Increase vegetables for fiber
Increase fish, nuts for omega 3s
Reduce simple carbs & sugar
Concentrate flavors to be satisfied with smaller portions

The Mediterranean diet is lower in “Advanced glycation endproducts” (AGE!) & lowers risk for AD

Perrone & Grant. J Alzheimers Dis. 2015
Addition of carbohydrate or glucose to protein is glycation. Leads to stiffening tissues, cells & arteries.

AGEs reduced by:
- Cooking with moist heat
- Shorter cooking times
- Lower temperatures
- Addition of lemon juice or vinegar

Mark et al Consumption of a diet low in advanced glycation end products for 4 weeks improves insulin sensitivity in overweight women. Diabetes Care. 2014
The B vitamins

Co-enzymes for energy production.

Vitamin B$_1$ (thiamine)
Vitamin B$_2$ (riboflavin)
Vitamin B$_3$ (niacin)
Vitamin B$_5$ (pantothenic acid)
Vitamin B$_6$ (pyridoxine)
Vitamin B$_7$ (biotin)
Vitamin B$_9$ (folic acid)
Vitamin B$_{12}$ (cobalamins)

Omega 3 is found in fish, fish oil, winter squash, flaxseed, & nuts. Lowers risk of cardiovascular disease, & diabetes. Lowers risk of AD by increasing brain-derived neurotrophic factor (BDNF).

Caloric Restriction (CR)

CR triggers “autophagy” which clears old proteins & cellular debris

Consider intermittent fasting – one day a month?

Do not eat for 12 hours between dinner & breakfast; do not eat within 3 hours of sleep

Or reduce calories + increase exercise

Spilman et al Inhibition of mTOR by rapamycin abolishes cognitive deficits and reduces amyloid-beta levels. PLoS One. 2010
High homocysteine (HC) found in AD – have level determined.

HC from the sulfur-containing amino acid methionine

Lower HC by increasing B6/B12 & folic acid

Sugar induces insulin production. Insulin is degraded by neprilysin & insulin degrading enzyme, competing with Aβ.

Adult-onset diabetes a risk factor for AD. Keep glycemic index low.

Chronic dehydration can impair mental function & normal digestion.

Older people at risk for dehydration due to low water consumption, chronic illness & certain medications.

Consume some electrolyte (but low sugar)-containing liquid.

Accurate Diagnosis is Critical

Diagnostics include:

- Computer-assisted tomography (CAT) for structural abnormalities
- Positron emission tomography (PET) for glucose use and amyloid imaging
- Function magnetic resonance (fMRI) for blood flow
- Tests of cognitive function

Other causes of memory loss:
- Depression, infection, multiple sclerosis, low B12, hypothyroidism, medication interactions, tumor

Not all dementia is AD:
- Vascular dementia, Parkinson’s disease, frontotemporal dementia

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