DEMENTIA DEMYSTIFIED

PRACTICAL APPLICATIONS FOR PREVENTING AND REVERSING COGNITIVE DECLINE WITH FUNCTIONAL MEDICINE

KAT TOUPS, MD, DFAPA, IFMCP

FUNCTIONAL MEDICINE PSYCHIATRY AND DEMENTIA

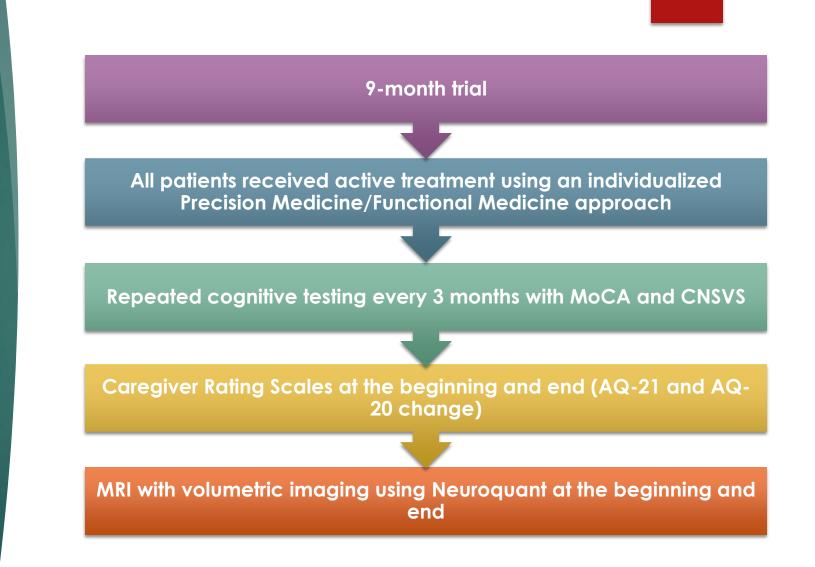
DEMENTIA DEMYSTIFIED PRACTICAL APPLICATIONS FOR PREVENTING AND REVERSING COGNITIVE DECLINE WITH FUNCTIONAL MEDICINE

- ► Kat Toups, MD, DFAPA, IFMCP
- Functional Medicine Psychiatry and Dementia
- ▶ Walnut Creek, CA
- www.BayAreaWellness.net
- www.DementiaDemystified.com

DEMENTIA IS BOTH PREVENTABLE AND TREATABLE WHEN WE FIND AND CORRECT THE UNDERLYING CAUSES

Dementia is NOT A DEATH SENTENCE

Prospective clinical trial with 25 patients MCI (Mild Cognitive Impairment) or Early Dementia Impairments in CNS Vital Signs Neuropsych testing (2 subtests < 50th percentile) And/or MoCA (Montreal Cognitive Assessment) >18 Investigators: Kat Toups, Ann Hathaway, Deborah Gordon + Dale Bredesen as advisor



STUDY PROCEDURES - DIET

Ketogenic Diet with at least mild ketosis

Grain Free, Dairy Free, whole foods organic Paleo-type diet (lots of vegetables, healthy fats, and a little free-range meat/chicken/fish)

Time Restricted Eating/Intermittent Fasting – restrict calories to 8 – 12 hours a day

Avoid eating 2 - 3 hours before bedtime.



STUDY PROCEDURES - OTHER

SLEEP OPTIMIZATION – including assessment and treatment of Sleep Apnea

·|--||

EXERCISE – combo of strength and balance training, aerobics, and HIIT (High Intensity Interval Training)

BRAIN TRAINING – Brain HQ



MINDFULNESS TRAINING/STRESS REDUCTION – HeartMath



DENTAL HEALTH – Dentalcidin Toothpaste and Dental Rinse from Bio-Botanical Research

STUDY PROCEDURES – SUPPORT TEAM

NUTRITIONIST

HEALTH COACH – went to the patient's home

EXERCISE COACH

STUDY PARTNER – usually a spouse or adult child living in the home

STUDY PROCEDURES – TESTING

TESTING – Large battery of tests including:

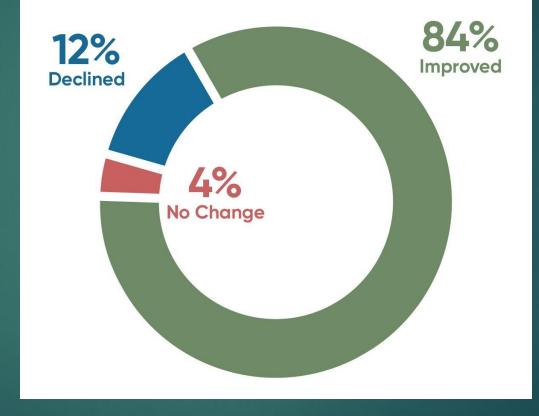
- Nutrients, Omega Fatty Acids, Metals (Genova NutrEval)
- Cardio-metabolic, inflammatory, and immune markers
- Hormones
- Infections including tick-borne illness from Armin Labs
- Mycotoxins, Chemical Toxins, Organic Acids from Great Plains Labs
- Home Mold Testing Mycometrics ERMI
- MARCoNS Nasal Testing Microbiology Dx
- Comprehensive Stool Analysis from Doctors Data
- Genetics Intellxx DNA

STUDY PROCEDURES – TREATMENT

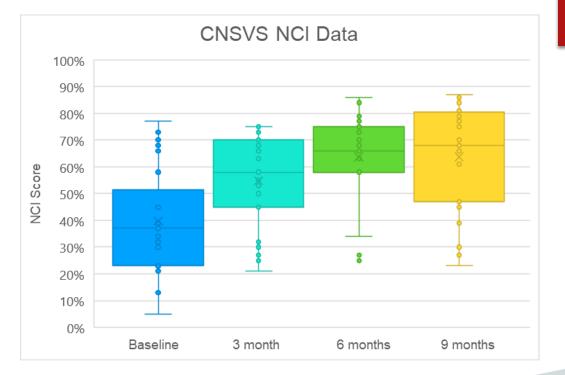
- We used some basic nutrients for nutritional and mitochondrial support, plus some nootropic support.
- All hormones were optimized.
- Beyond that, treatments for each patient were individualized, based on their findings with the testing and assessments.

Clinical Trial Results

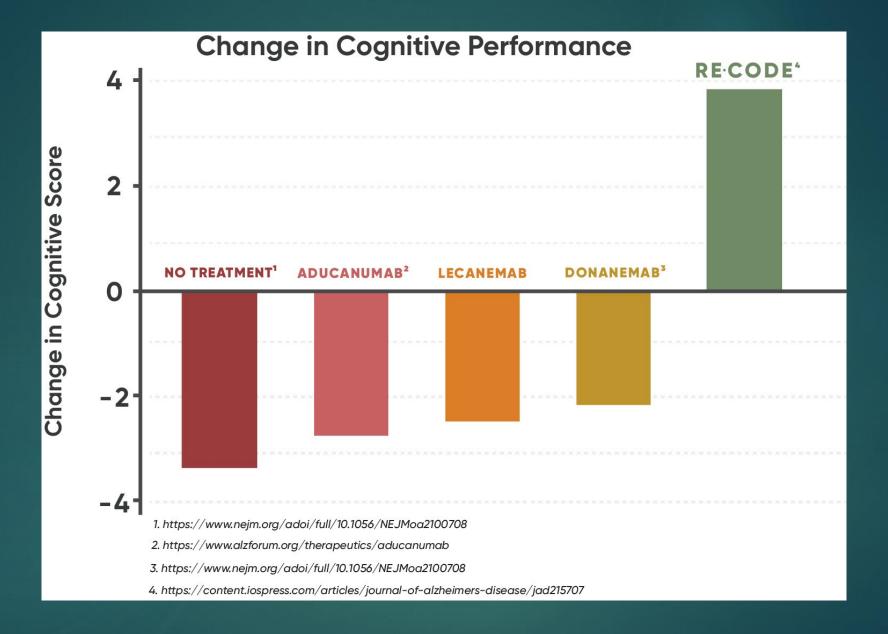
effect on participants' cognition







4 Winds Clinical Trial Results



4 Winds Clinical Trial Results

BRAIN MRI VOLUMETRIC CHANGES

No brain volume loss or cortical thinning was detected in the trial participants

GRAY MATTER VOLUMES

- Study Subjects *increased* by a mean of 0.3%
- Normal Controls *decrease* by 0.83-0.92%
- Alzheimer's Patients *decrease* 2.20-2.37%

HIPPOCAMPAL VOLUMES

- Study Subjects *decreased* **1.29%**
- Normal Controls *decrease* 1.41-1.73%
- MCI or Alzheimer's *decrease* 3.5-4.66%

OTHER "SIDE EFFECTS" IMPROVEMENTS IN:

- Weight, waist circumference, BMI
- Strength and Fitness
- Blood Pressure
- Lipids
- Glucose levels
- hsCRP
- Autoimmunity

ALZHEIMER'S DISEASE IS A NEURODEGENERATIVE DISORDER – BUT NOT A MYSTERIOUS, UNTREATABLE BRAIN DISORDER.

- It is a reversible multisystem illness that occurs due to toxins and infections and inflammation and lack of hormones and other diet and lifestyle factors.
- It can have a strong auto-immune component as well.

THERE ARE REASONS NEURODEGENERATION HAPPENS

WHEN WE FIND AND ADDRESS ALL OF THE DRIVING FACTORS, WE GAIN TRACTION IN STOPPING AND REVERSING THE DEGENERATIVE PROCESS.

ALZHEIMER'S IS A MULTI-FACTORIAL DISEASE

CONTRIBUTING FACTORS IN DEMENTIA:

METABOLIC, NUTRITIONAL, TOXIC, INFLAMMATORY, INFECTIOUS, AUTOIMMUNE, CHRONIC STRESS, HEAD TRAUMA, AND/OR WITHDRAWAL OF TROPHIC HORMONES

NEUROPLASTICITY:

THE AMAZING CAPACITY OUR BRAIN HAS FOR REGENERATION WHEN WE REMOVE THE OFFENDING FACTORS.

FUNCTIONAL MEDICINE + PRECISION MEDICINE

► FM SEEKS TO DISCOVER THE ROOT CAUSES OF ILLNESS

- ASKS WHY WHY DOES THE PERSON HAVE THIS DISEASE? WHAT HAS CAUSED IT?
- PRECISION MEDICINE: PERSONALIZED MEDICINE THAT TARGETS THE RIGHT TREATMENTS TO THE RIGHT PATIENT AT THE RIGHT TIME

NOT A PILL FOR AN ILL

- ▶ IN PSYCHIATRY AND NEUROLOGY, WE ARE TAUGHT TO GIVE A PILL FOR AN ILL.
- BUT THE ANSWER TO GETTING WELL WITH A MULTI-FACTORIAL ILLNESS IS NOT GOING TO BE FOUND IN A PILL.
- MONOTHERAPUETIC AGENTS LIKE ANTI-AMYLOID DRUGS HAVE NOT BEEN SUCCESSFUL AT IMPROVING COGNITIVE DECLINE.
- ► THE BRAIN IS NOT SEPARATE FROM THE BODY.
- ▶ WHAT HAPPENS IN THE BODY IS WHAT HAPPENS IN THE BRAIN!

SENIOR MOMENTS

- Word-Finding Difficulty or Saying the Wrong Word
- Forgetting People's Names or Dropping the Ball on Tasks
- Forgetting Details of Recent Events or Travel (or yesterday's conversation)
- Misplacing or Losing Things
- Trouble with Directions or Getting Lost; Over-Reliant on GPS
- Trouble with Math (like calculating a tip)
- Following Recipes stressful / General Overwhelm

WHAT DOES THE DOCTOR SAY?

IT'S NORMAL TO HAVE SOME CHANGES IN YOUR MEMORY WITH AGING

- THERE'S NOTHING TO WORRY ABOUT
- ► WRONG!!

SUBJECTIVE COGNITIVE IMPAIRMENT (SCI) – CAN START YEARS OR DECADES BEFORE MCI AND DEMENTIA.

MEMORY DECLINE – 3 YEARS

2016.11.28 NEUROPSYCH Immediate Memory 73% Delayed Memory 18% Language 53% Total 79% 2019.11.27 CNSVS TESTING Verbal Memory 7% (92% at end of 9-month Study) Composite Memory 21%

ALZHEIMER'S DEMENTIA

- Alzheimer's Dementia is a Neurodegenerative Disorder characterized by Amyloid Plaques (aka A-beta) and Neurofibrillary Tangles (aka Tau-beta).
- Amyloid Hypothesis is not useful for treatment Amyloid is a downstream effect.
- Amyloid is secreted to protect the brain tissue in response to a hostile provocation.
- Treatment goal is to stop the attack, rather than remove the Amyloid, which does not translate into any improvement clinically.

GENES THAT LEAD TO A MORE EXUBERANT AMYLOID RESPONSE

Apo E4 (Apolipoprotein E4) – 25% have 1 copy, 2-3 % homozygous

Presenilin-1 (PS1)

Amyloid Precursor Protein (APP)

ALZHEIMER GENETICS: GENES DO NOT EQUAL DESTINY!

- We have control of the epigenetic factors that turn the genes on and off and cause deposition of the Amyloid that leads to plaques.
- ApoE4 carriers have a more exuberant amyloid response to provocation or injury than E2 or E3.
- So with E4, need to work harder to mitigate triggering factors.

APOE4 GENE MODIFIERS – DECREASE APOE4 DEMENTIA RISK

- TOMM40 and ApoC1 alleles significantly increase AD risk (independent of ApoE4).
- If no TOMM40 or ApoC1, the risk of Apo4 is lowered to very close or equal to Apo 3/3.
- ApoE4 R251G reduces risk of AD by more than 60% + 6-year delay in onset
- ApoE3 V236E reduces risk of AD by more than 50% + 10-year delay in onset
- BCHE K variant negative halves the risk of Apo E4
- Conversely, BCHE K variant positive doubles the risk.

3 RS OF MY DEMENTIA PROGRAM

- REMOVE THE FACTORS WEAKENING OR HURTING THE BODY AND BRAIN
- **REPLACE** NUTRIENTS AND HORMONES
- REGENERATE THE BRAIN TO REGROW DAMAGED NEURONAL CONNECTIONS

FIRST R: REMOVE

► INFECTIONS

- ► TOXINS/MYCOTOXINS (MOLD)/METALS
- HIGH BLOOD SUGAR
- ► HIGH LIPIDS
- ► INFLAMMATION
- ► IMMUNE PROBLEMS

13 MODIFIABLE RISK FACTORS

- Mid-Life Hearing Loss
- Education
- Traumatic Brain Injury
- ► Hypertension
- Physical Inactivity
- Diabetes
- Gum Disease

- Excessive Alcohol Consumption
- Weight Control and Obesity
- Smoking
- Depression
- Social Contact
- Air Pollution

CAST A WIDE NET WITH TESTING

- ► NO TIME TO LOSE WITH DEMENTIA
- TEST EVERYTHING AS FAST AS POSSIBLE BY CASTING A WIDE NET
- ► THIS GIVES TREATMENT TARGETS! MUST FIX THEM ALL.
- INFECTIONS, TOXINS, MOLD, HORMONES, THYROID, IMMUNE, BLOOD SUGAR CONTROL, ADVANCED LIPIDS, INFLAMMATION, CLOTTING FACTORS

HPA AXIS DISRUPTED BY:

- ► Infections
- Mycotoxins
- Head Trauma
- Chemical Toxins
- Heavy Metals
- Lack of trophic hormones

INFECTIONS LINKED WITH COGNITIVE DECLINE

- LYME
- BABESIA
- BARTONELLA
- EHRLICHIA/ANAPLASMA
- TICK BORNE RELAPSING FEVER SYPHILIS
- EBV + EAD •
- HSV 1/2
- HHV-6
- HHV-7

- TOXOPLASMOSIS
- MYCOPLASMA
- CMV
- CHLAMYDIA
- HIV
- HEPATITIS
- COVID

INFECTIONS INFLAME AND DISRUPT THE HPA AXIS AND AFFECT HORMONE LEVELS

I-Cubed: Inflammation/Infection/Immune

- The immune activation (inflammatory cytokines) to fight the infections can result in deposition of amyloid plaques to protect vulnerable neurons from damage.
- A little amyloid is protective, but chronically it will cause destruction and death of neurons.
- It is not uncommon to see abnormal hormone levels even in young people with brainbased infections like Lyme Disease or Mycotoxin illness from neuronal destruction.

VIRUSES & DEMENTIA

- Two papers published in 2018 in Neuron have implicated herpesviruses HHV-6A, HHV-7 and HSV1 in the development of Alzheimer's.
- HHV-6A, in particular, was found to be a key viral modulator in AD.
- These viruses accelerate β amyloid deposition and induce tau β fibrillization
- Progression of AD correlates with increased levels of HSV1, HHV-6, and HHV-7 across multiple brain regions.
- A third 2016 paper: J of Alzheimer's Disease when HSV patients are treated with antiviral medications, the relative risk of dementia was reduced by a factor of 10.

Readhead et al. – Multiscale Analysis of Independent Alz Cohorts Finds Disruption by ... Human Herpesvirus – Neuron. Volume 99, 2018 Eimer et al. – Alzheimer's Disease-Associated B-Amyloid is Rapidly Seeded by Herpesviridae to Protect Against Brain Infection – Neuron. Vol 99, 2018 Ruth Itzhaki et al – Microbes and Alzheimer's Disease – Journal of Alzheimer's Disease Vol 51, no 4, pp 979-994, 2016.

WHERE TO TEST INFECTIONS

- All of the infections on the previous slides can be tested at Quest or Lab Corp, other than the tick-borne infections that are not reliable there.
- Quest and LabCorp do not test the Lyme bands that were impacted by the Lyme vaccine, and they only test single strains of Lyme and co-infections.
- For Tick-borne disease, I use Igenex (covered by Medicare other than FISH tests), InfectoLab (T-Cell testing – no insurance), and sometimes MDL for Western Blot since they take insurance (but they do not test multiple strains, so more false negatives).

DENTAL INFECTIONS

Gum Disease for 10 years -- 70% more likely to develop Alzheimer's
 Important to also assess hidden infections, like hidden caries, occult root canal infections, and possible cavitations that will trigger the immune system.

CBCT (Cone Beam CT Scan) – read by Dental Radiologist

 Home Dental Pathogen Testing: My PerioPath (OralDNA.com) – 11 dental pathogens DirectDiagnostics.com – 5 dental pathogens Bristle Health SimplyPERIO – tests viruses (EBV, CMV, HSV) in addition to dental pathogens

NASAL INFECTIONS

- Infections in the nose and sinuses can travel across the porous cribriform plate at the back of the nose and into the brain.
- Covid known to do this affects the olfactory nerves (impaired smell) as well as causing both brain fog and dementia symptoms.
- Mycotoxins (from mold) are also believed to impact the brain via this route. Several mycotoxins are neurotoxic, like Ochratoxin (linked to Alzheimer's and Parkinson's) and Aspergillus (gliotoxins) linked to neurologic impairment.
- See RESOURCES 2 slide for where to test (Microbiology Dx).

LYME DISEASE

- LYME LOVES TO LIVE IN THE BRAIN AND NERVE ROOTS.
- ► LYME IS A SPIROCHETE JUST LIKE SYPHILIS.
- BOTH CAN MIGRATE TO THE BRAIN AND CAUSE DEMENTIA OVER TIME.
- ► LYME ALSO SUPPRESSES THE IMMUNE SYSTEM.
- MANY PEOPLE WITH LYME HAVE NO MEMORY OF A TICK BITE, SO IT MUST BE TESTED AS PART OF A DEMENTIA WORK-UP.
- LYME COINFECTIONS LIKE BABESIA AND BARTONELLA ALSO CAUSE NEUROPSYCHIATRIC SYMPTOMS, AND MUST ALSO BE TESTED.

CHEMICAL TOXINS & HEAVY METALS

- Disrupt the brain function and HPA Axis
- Activate the immune system
- Cause cancer, endocrine disruption, neurodegeneration
- Infants today are born with over 200 chemicals in their blood from their mother's exposures.
- Accumulation is complicated by genetic mutations and snps that affect detoxification. Poor detoxifiers genetically accumulate more.

OTHER TOXINS: POLLUTION

Mexico City: Even the dogs have a dementia problem!

- 2019 study of autopsies age 11 months 40 years found 99.5% had levels of beta-Amyloid and phosphorylated Tau above normal.
- Even the 11-month-old baby!
- First Responders and people living near 9/11 Ground Zero are also manifesting higher levels of early-onset dementia.
- Remember that ApoE4 carriers will make more Amyloid in response to these inhaled toxins, so they need more aggressive detox with exposures.

DETOX OF METALS AND CHEMICALS

- High Mercury: Avoid all seafood (other than scallops and deveined shrimp) for 4-6 months to lower Mercury levels.
- Use liver support like Sulphoraphanes (Broccoli extract) to upregulate Phase 2 liver detox enzymes.
- Sauna/Sweating can detox metals, chemicals, and mycotoxins. (Be sure to wipe off sweat and shower afterwards so toxins are not reabsorbed.)
- Binders : Charcoal, Clay, Chlorella, Cholestyramine, Modified Citrus Pectin
- Other Metal Chelation protocols with DMSA or EDTA.
- Can see rapid improvement in cognition for some people, especially when chelating high lead levels.

SAUNA REDUCES ALZHEIMER'S RISK

- 2018 study in Finland showed elderly men using daily sauna had a much lower incidence of Alzheimer's than those using 3 times a week.
- 3 times a week sauna users had a 21% lower incidence of Alzheimer's than those using the sauna once a week.
- The overall dementia risk for those using for 15 minutes or more, 4-7 times a week, was 66% less!
- Studies show regular sauna use is associated with reduced risk of coronary diseases, sudden cardiac death, stroke, hypertension, respiratory diseases, lower CRP, and reduced rates of Alzheimer's Disease and Dementia.

Tanjaniina Laukkanen, et al. Sauna bathing is inversely associated with dementia and Alzheimer's disease in middle-aged Finnish men. Age and Ageing, December 2016 DOI: 10.1093/ageing/afw212

MYCOTOXINS FROM TOXIC MOLD

- Many people can clear mycotoxins easily not a problem for everyone.
- Some cannot eliminate the mycotoxins, which stay in the body and keep triggering the immune system.
- Inhaled mycotoxins can travel through the porous cribriform plate at back of nose to the brain, leading to neurologic symptoms including impaired cognition and neurodegeneration.
- Can test neuropeptide levels affected by mycotoxins and/or Lyme (CIRS Labs – chronic inflammatory response system) – Quest and LabCorp – like TGF-b1, MMP-9, VEGF, MSH, and urine Mycotoxin levels at Great Plains Lab (now Mosaics) or Real Times Lab.
- I have had patients unable to talk or feed themselves recover after removing and treating for mold.

HOME DUST TESTING FOR MOLD/MYCOTOXINS

www.LisBiotech.com ERMI Dustcloth - \$240 **Provides both ERMI and HERTSMI scores** Mycometrics.com <u>ERMI - \$300</u> HERTSMI - \$150 Best to order the dustcloth (rather than the Vacuum canister) www.MyHouseMakesMeSick.com – to score the Mycometrics testing for a Moldiness Index of your home. You upload the scores from Mycometrics testing to this program for a General Moldiness Index called a HERTSMI-2 score.

AGING: DECLINE IN IMMUNE FUNCTION

- ► AGING AND STRESS BOTH SUPPRESS THE IMMUNE SYSTEM.
- ► ALLOWS LATENT VIRUSES TO "WAKE UP" or REACTIVATE
- ▶ SOME INFECTIONS, LIKE LYME DISEASE, WILL FURTHER SUPPRESS THE IMMUNE SYSTEM.
- IMMUNE SYSTEM REACTS BY MAKING INFLAMMATORY CYTOKINES TO KILL THE INVADING BRAIN INFECTIONS.
- RESULTING NEUROINFLAMMATION WILL DESTROY HEALTHY BRAIN CELLS = NEURODEGENERATION
- WANT TO REMOVE ANYTHING TRIGGERING THE IMMUNE SYSTEM, INCLUDING FOOD ALLERGIES.

YOUR BRAIN ON SLEEP

- OUR BRAINS DETOXIFY AND RESTORE DURING SLEEP.
- ► GLYMPHATICS SYSTEM FOR BRAIN DETOX IS ACTIVATED DURING **DEEP SLEEP**.
- ► 6 HOURS/NIGHT SLEEP CHEATS THE BRAIN OF DETOX:
 - = 14 HOURS/WEEK LESS DETOX
 - = 60 HOURS/MONTH LESS DETOX
 - = 720 HOURS/YEAR LESS DETOX

SLEEP APNEA

- DEPRIVES THE BRAIN OF OXYGEN ALL NIGHT
- BRAIN AND HEART ARE HIGHEST CONSUMERS OF OXYGEN, SO THEY SUFFER MOST
- CAUSES DEATH OF BRAIN CELLS AND A STRAIN ON THE HEART THAT LEADS TO CONGESTIVE HEART FAILURE
- SLEEP APNEA OCCURS IN THIN WOMEN WITH NO SNORING DO NOT HAVE TO BE MALE OR OVERWEIGHT. MIGHT HAVE UARS – Upper Airway Restriction Syndrome.
- SCREEN WITH HOME TESTING FOR 3 NIGHTS (see Resources for options)

LAB TESTING

- Advanced Lipid Profile with lipid sub-particles (CardioIQ inflam)
- Glucose/Blood Sugar control: Hemoglobin A1c, fasting insulin, fasting glucose + advanced diabetes markers (will pick up early diabetes risk)
- Inflammation advanced inflammation markers (hsCRP, PLA-2, MPO, Fibrinogen)
- Hormones Sex hormones and Thyroid hormones with antibodies
- Vitamin and Mineral levels
- Infections that affect the brain: Lyme, Lyme co-infections, Mycoplasma, HIV, Syphilis, Toxoplasmosis, Epstein Barr Virus (EBV), Cytomegalovirus (CMV), Herpes Simplex 1/2, Human Herpes Virus (HHV-6, HHV-7), Hepatitis, Chlamydia, Mycotoxins (mold), ...
- Genetics: ApoE Alzheimer's gene, MTHFR methylation genes, Clotting Factor Mutations (Factor V Leiden & Prothrombin), Detox genes if indicated
- Heavy Metals testing whole blood levels (avoid fish before testing mercury)
- Chemical Toxin and Glyphosate (Round-Up) testing
- Comprehensive Stool Analysis with Parasitology x 3
- MARCoNS testing for bacterial infections and fungus in nose (Microbiology Dx) optional if persistent sinusitis or mold
- Sleep Apnea and/or High Intensity Pulse-Ox home testing
- MRI Brain for NeuroQuant or NeuroReader (volumetric measurement of the brain structures)

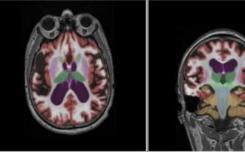
NeuroQuant[®] Triage Brain Atrophy Report

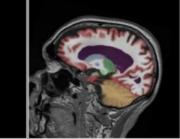
RDT - SOCAL 1516 Cotner Ave Los Angeles, CA 90025

PATIENT INFORMATION

PATIENT INFORM	ATION			Version 3.0.1
Patient ID:	Patient Name:		Referring Physician: TOUPS, KATHLEEN	
SCAN INFORMATI	ON			
Scan Date: 2022-01-09		Accession Number: 30970786		

MORPHOMETRY RESULTS





					Percentiles		
				Cortical Brain Regions	Left	Right	Tota
Structure	Total Vo	lume	Percentile	Frontal Lobes	28	28	27
Structure	(cm ³)		Percentile	Superior Frontal	8	20	11
Intracranial Volume	1590			Middle Frontal	51	34	41
Whole Brain	Whole Brain 1178		50	Inferior Frontal	11	13	10
Forebrain Parenchyma	1017		47	Lateral Orbitofrontal	87	61	78
	Percentiles			Medial Orbitofrontal	58	48	51
Total Volumes	Left	Right	t Total	Paracentral	88	56	80
Cerebral White Matter	71	72	71	Primary Motor	42	75	61
Cortical Gray Matter	23	25	24	Parietal Lobes	81	46	66
Ventricles	99		99	Primary Sensory	38	47	41
Cerebral WM			20	Medial Parietal	99	99	99
Hypointensities*		21	29	Superior Parietal	43	26	31
Subcortical Structures				Inferior Parietal	79	46	65
Cerebellar White Matter	er 98 88		95	Supramarginal	16	13	10
Cerebellar Gray Matter	r 59 45		52	Occipital Lobes	63	80	73
Brainstem		-	2	Medial Occipital	90	95	94
Thalamus	1	5	2	Lateral Occipital	33	45	35
Ventral Diencephalon	7	5	4	Temporal Lobes	1	2	1
Basal Ganglia				Transverse Temporal +	1	1	1
Putamen	86	72	82	Superior Temporal			
Caudate	99 99 99			Posterior Superior Temporal Sulcus	26	52	39
Nucleus Accumbens	59	18	37	Middle Temporal		3	
Pallidum	14	4	6	Inferior Temporal	-	10	-
Cingulate	97	99	99	Fusiform	3	27	10
Anterior Cingulate	91	91 99 99		Parahippocampal	60	56	58
Posterior Cingulate	osterior Cingulate 86 92 90		90	Entorhinal Cortex	19	10	12
Isthmus Cingulate	84	60	76	Temporal Pole	34	25	27
					50	77	65
				Amygdala	50	48	22
				Hippocampus			

*White matter hypointensities are abnormally low signal intensity regions within white matter as observed on a T1-weighted MRI scan.

BRAIN BIOMARKER TESTING - PLASMA

Amyloid

- Looks at Ratio of AB42/AB40 in plasma
- Generally covered by insurance at Quest
- Quest: AD Detect; Precivity AD

Phosphorylated Tau

- Correlates with amyloid plaques and neurofibrillary tangles in brain.
- Much more sensitive than plasma amyloid for detecting neurodegeneration.
- Two markers: pTau -181, pTau-217 (217 more sensitive in early AD)
- LabCorp, Quest, and NeuroCode all test pTau-181 and pTau-217

Neurofilament Light Chains (NfL)

- Marker of neuronal injury that correlates with amyloid and tau levels.
- Currently at LabCorp and NeuroCode; soon at Quest
- 10% higher in AM than PM

Glial Fibrillary Acidic Protein (GFAP)

- Non-specific marker of astrocyte/glial degeneration.
- Available at NeuroCode.

MICRONUTRIENT AND METALS TESTING

- Genova NutrEval is an excellent panel that tests for all kinds of nutrient levels (including mitochondrial nutrients and omega fatty acid levels), some metal and chemical toxin levels, organic acids, and more.
- NutrEval is covered by Medicare with appropriate diagnostic codes.
- Quest is now offering panels for: Antioxidants, B Vitamins, Minerals, and Heavy Metals.
- LabCorp has a Trace Minerals panel as well as Heavy Metals testing.

SECOND R: REPLACE

- IN ADDITION TO REMOVING THE BAD STUFF (TOXINS, INFECTIONS, METALS, MYCOTOXINS), WE NEED TO REPLACE BOTH NUTRIENTS AND HORMONES TO OPTIMIZE OUR BODY FUNCTIONING.
- EASY TO MEASURE THE NUTRIENTS AND HORMONES, AND THEN REPLACE TO OPTIMAL LEVELS
- OPTIMIZE DIET, SLEEP, EXERCISE, STRESS REDUCTION, IMMUNE FUNCTION
- OPTIMIZE BRAIN INPUTS: VISION, HEARING, SMELL

FORTIFY YOUR IMMUNE SYSTEM

- EAT WELL/SLEEP WELL/EXERCISE/REDUCE STRESS
- AVOID SUGAR
- CARBS = SUGAR
- ELIMINATE GLUTEN; PREFER ALL GRAINS DUE TO HIGH GLYCEMIC INDEX
- EAT ORGANIC, FREE-RANGE, NON-PROCESSED FOOD
- LOTS OF HEALTHY FATS FOR THE BRAIN
- LDN (Low Dose Naltrexone) sometimes used for immune support

DETOX: A LIFELONG ENDEAVOR

- ► THE WORLD HAS BECOME INCREASINGLY TOXIC.
- ▶ DETOXIFICATION IS NOT JUST A ONE-AND-DONE TREATMENT; NEEDS TO BE ONGOING.
- ► IMPORTANT TO ASSESS LEVELS OF METALS AND CHEMICAL TOXINS
- SOME WILL NEED MORE AGGRESSIVE DETOX, BUT EVERYONE BENEFITS FROM REGULAR DETOX PRACTICES.
- ▶ ELIMINATE TOXINS IN THE HOME AND EAT AS ORGANIC/FREE RANGE AS POSSIBLE.
- ► SAUNA/SWEATING HAS GREAT DATA FOR DETOX.
- SULPHORAPHANE (BROCCOLI EXTRACT) IS HELPFUL TO UPREGULATE DETOX ENZYMES AND DECREASE NEUROINFLAMMATION.

NUTRIENT DEFICIENCIES THAT INCREASE DEMENTIA RISK

B12, B1, B3, B6

- VITAMIN D
- VITAMIN C
- VITAMIN E
- MAGNESIUM

- ZINC
- COPPER
- IRON
- FISH OIL
- COQ10

3 CORE SUPPLEMENTS

- FISH OIL 3 GRAMS A DAY (make sure the brand is pure/non-toxic)
- B COMPLEX or Multivitamin
- VITAMIN D LEVEL 50-80
- ADDITIONAL B12 if needed
- MTFH (methyl folate) if Methylation support is needed

NEURODEGENERATION & MITOCHONDRIA

- With any degenerative disease, the mitochondria are under siege, so adding key nutrients for mitochondrial support is always helpful.
- Amyloid inhibits the electron transport chain in mitochondria, so mitochondrial support becomes essential with Alzheimer's or any type of neurodegenerative disorder.
- I like to use supplements like Co-QIO, Acetyl L-Carnitine, NAC and/or Glutathione, and R-Lipoic Acid for mitochondrial support.
- Co-Q10 is essential for mitochondrial support as it's required for one of the final steps to make ATP for cellular energy in the electron transport chain.

MITOCHONDRIAL NUTRIENTS

- CoQ10
 Acetyl L-carnitine (alcar)
 R-Lipoic Acid
 NAC (N-Acetyl Cysteine)
- Glutathione
 PQQ
 Vitamin K (MK7)
 Shilajit

HORMONES IN THE BRAIN

Neuroprotective (trophic for the brain)
 Neurosteroids
 Neurotransmitters

HORMONE BRAIN RECEPTORS

Estrogen
Progesterone
Testosterone
Pregnenolone
DHEA

Thyroid Hormones

Vitamin D

Vitamin B12

Cannabinoids

BDNF (Brain Derived Neurotrophic Factor)

NEUROSTEROIDS: BRAIN PRODUCES ITS OWN HORMONES

- Hypothalamic neurons make their own supply of Estrogen!
- There are many estrogen receptors in the brains of men and women.
- Estrogen acts as a neurotransmitter in the brain, and influences emotions, mood, and cognitive function.
- E2 also increases cerebral perfusion by binding endothelial receptors and stimulating Nitric Oxide release for vasodilation.

ESTROGEN IN THE BRAIN

Shuttles Glucose into Brain

- Binds receptors in prefrontal Cortex, Hippocampus, Basal Forebrain, and Striatum
- Essential for consolidation of memories

Produced in the Hypothalamus, even after menopause or andropause

ESTROGEN AND COGNITIVE DECLINE

- Lack of Estrogen leads to cognitive decline and neurodegeneration in some women.
- Natalie Rasgon, MD at Stanford (2014): randomized women with Alzheimer's risk on HRT x 10 years to stop or continue; followed for 2 years
- Women randomized to stop the hormones all exhibited a significant decline on FDG-PET scan of their frontal and posterior cingulate metabolism – two areas that decline early in Alzheimer's.
- Women who continued their hormone replacement had preservation of their frontal and posterior cingulate metabolism with no observable changes (unless they used synthetic Progestin, which negated the Estradiol advantages).

PROGESTERONE AS NEUROSTEROID

- Progesterone is also a neurosteroid, important for myelin production and neuroprotection.
- Synthesized locally in the nervous system by glial cells and neurons.
- In addition, Progesterone made in the periphery (ovaries and adrenals in women; adrenals in men) can easily cross the BBB.
- Progesterone is converted to allopregnanolone, which binds to GABA receptors in the brain helps sleep, anxiety, and memory.

PROGESTERONE – TBI & STROKE

- Progesterone affects Myelin Production
- Promotes growth and repair of Myelin sheath after injury
- Progesterone production is upregulated after TBI, and there is data for supplemental Progesterone after ischemic stroke.
- High-Dose Progesterone for 3 days after TBI or Stroke helpful for decreased mortality and better cognitive recovery.

TESTOSTERONE

- Testosterone boosts Dopamine our "feel-good" hormone and protects against Depression. It helps sleep as well.
- Testosterone is important for motivation, cravings, and desire.
- Confers cardiovascular protection, protects bone density, maintains lean muscle mass
- Produced by the testicles, ovaries, and adrenal glands.
- Testosterone optimization can alleviate depression as well as improve cognition and memory – in women and men.
- Replacement in women is available through compounding pharmacies.

HORMONES ARE TROPHIC FOR THE BRAIN

- Many studies show evidence of the trophic nature of these hormones for the brain and cognition.
- Also, studies supporting the use of hormones for healing from TBI and stroke.
- Easy to test all of these various hormones and replace the levels to the mid-point of a therapeutic range.
- Estrogen, Progesterone, Free and Total Testosterone, Pregnenolone, DHEA-S, TFTs

REPLACING BIOIDENTICAL HORMONES

- Measure blood levels after starting to assure patients are in a therapeutic range.
- Transdermal bioidentical estrogen does not increase risks for breast and uterine cancer or blood clots. Avoid oral, as first-pass metabolites can be carcinogenic.
- New studies are showing that bioidentical Estrogen and Progesterone might actually be protective for these types of cancers, even when a woman has already had breast cancer.
- Bioidentical Estrogen and Progesterone are now easily available as generic prescriptions. (Medicare does not cover, so have patients use GoodRx coupon.)

OPTIMIZE BLOOD SUGAR AND LIPIDS

- Heart health = Brain health
- Whatever happens to the heart and blood vessels is also affecting the brain.
- ▶ What's good for the heart is good for the brain. Same thing for what is bad ...
- Controlling lipids, blood pressure, insulin resistance, and blood sugar levels are imperative to save the brain.
- Dementia is also known as Type 3 Diabetes. Insulin resistance leads to oxidative stress and free radicals that damage neuronal cell membranes, as well as causing vascular damage that affects circulation/perfusion.

CHOLESTEROL IS NOT THE ENEMY

HEALTHY TYPE OF FAT LIPOPROTEIN

- CHOLESTEROL IS PRECURSOR TO SEX HOMRONES, STRESS HORMONES, THYROID HORMONES
- IMPORTANT FOR BRAIN FUNCTION
- MYELIN SHEATHS THAT SURROUND NERVES AND HELP TO CONDUCT IMPULSES ARE MADE OF CHOLESTEROL – 80% lipids
- ► WHITE MATTER 60% lipids
- ► GRAY MATTER 40% lipids

HEALTHY FATS

► COCONUT

► AVOCADO

► FREE-RANGE MEAT, CHICKEN, EGGS

WILD-CAUGHT FISH

► NUTS

► SEEDS

TIME RESTRICTED EATING (TRE)

- ► LIMIT FOOD INTAKE TO 8-10-12 HOURS OF THE DAY
- CALORIE RESTRICTION PROMOTES LONGEVITY VIA AUTOPHAGY
- CAN LOWER BLOOD SUGAR
- CAN LOWER LDL CHOLESTEROL
- CAN REDUCE INFLAMMATION, INCLUDING NEUROINFLAMMATION
- BEST RESULTS WHEN EATING AT THE SAME TIME AND FASTING AT THE SAME TIME EVERY DAY

KETOGENIC DIET

- Ketosis: High Fat/Low Carb/Moderate Protein diet can be helpful with dementia.
- Used since 1920's for Kids with INTRACTABLE SEIZURES
- Ketosis can significantly reduce or eliminate seizures in many kids, and, can also be helpful with Schizophrenia and Bipolar Disorder.
- These conditions show a bioenergetic dysfunction with abnormal glucose utilization and mitochondrial dysfunction.
- Shifting from burning glucose to burning fat is a work-around for this.
- Ketosis can help with increased energy, brain clarity, and sometimes memory in adults.
- Follow advanced lipids after 3-4 months on a Keto diet, especially for people with Apo E4 alleles.

OPTIMIZE VISION, HEARING, AND SMELL

- Loss of Brain Input from decreased vision or hearing or smell results in less brain stimulation.
- Neurons that are not firing properly or stimulating the brain will be pruned out, leading to brain atrophy.
- Hearing Loss is the largest modifiable risk factor for developing dementia, exceeding smoking, hypertension, lack of exercise, and social isolation.
- Study of 16,000: A diagnosis of hearing loss between age 45 65 more than doubled the odds of a dementia diagnosis later in life.
- Retraining Smell Protocol Lemon, Rose, Eucalyptus, Clove Essential Oils

EXERCISE: REPLACE & REGENERATE

- Exercise is important for cardiovascular health, oxygenation and perfusion of the brain (and the rest of the body), stress reduction, and it increases BDNF.
- Women who exercised regularly in middle age (age 50) were 90% less likely to develop Alzheimer's in a 2018 study published in Neurology.
- Combination of strength and balance training, aerobics, and HIIT (High Intensity Interval Training).
- HIIT 3 times a week can improve mitochondrial levels, lower BP, improve blood sugar, and one study showed a 30% improvement in memory after just 12 weeks.

SLEEP & STRESS

- Psychiatrists already know the relevance of sleep and stress for the brain.
- Brain needs deep sleep to regenerate and detoxify.
- Cortisol is destructive to blood vessels and neurons, and chronic stress can double the risk of dementia.
- All people with memory problems must be screened for sleep apnea.
- Tracking sleep and HRV can be beneficial. Oura Ring, Garmin VivoSmart 4, Apple Watch are all useful options, and there are some free apps as well.
- Ketogenic Diet improves SWS and REM sleep.
- HeartMath standardized program we used in Dementia study to increase HRV, reduce stress, and improve sleep

THIRD R REGENERATE

- NEUROPLASTICITY: THE AMAZING CAPACITY OUR BRAIN HAS FOR REGENERATION WHEN WE REMOVE THE OFFENDING FACTORS
- GROW NEW NEURONS BY STIMULATING THEM
- EXERCISE AND MEDITATION BOTH INCREASE BDNF (BRAIN DERIVED NEUROTROPHIC FACTOR) THAT HELPS TO MAKE NEW BRAIN SYNAPSES

PROGRAMS FOR NEUROPLASTICITY

► EXERCISE

- MEDITATION/MINDFULNESS
- HEARTMATH MEDITATION FOR NON-MEDITATORS based on increasing Heart Rate Variability (HRV)
- BRAIN HQ BRAIN TRAINING on computer or cell phone app
- PHOTOBIOMODULATION LIGHT THERAPY Infrared Light wavelength 800 850 nm

PROMISING MITOCHONDRIAL TREATMENTS

- HBOT (Hyperbaric oxygen treatments)
- Photobiomodulation (Red Light/PEMF/Low Light Lasers)
- Neurofeedback
- IV NAD and SphenoCath NAD mitochondrial rejuvenation
- IV Stem Cells and Exosomes
- Plasma Exchange/Plasmapheresis

STUDY PAPERS: PRECISION MEDICINE APPROACH TO ALZHEIMER'S DISEASE: SUCCESSFUL PILOT PROJECT

KAT TOUPS, ANN HATHAWAY, DEBORAH GORDON, DALE BREDESEN, ET AL.

- Journal of Alzheimer's Disease August 2022
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9484109/
- Can also easily search web for the trial paper by putting in my name (Toups) + Precision Medicine

ADDITIONAL PAPERS – Journal of Alzheimer's Disease

Precision Medicine Approach to Alzheimer's Disease: Rationale and Implications

Bredesen, Toups, Hathaway, et al. Journal of Alzheimer's Disease, vol. 96, no. 2, pp. 429-437, 2023 <u>https://content.iospress.com/articles/journal-of-alzheimers-disease/jad230467</u>

Longitudinal White and Gray Matter Response to Precision Medicine-Guided Intervention for Alzheimer's Disease

Chaw, Raji, Toups, et al. Journal of Alzheimer's Disease, vol. 96, no. 3, pp. 1051-1058, 2023 <u>https://content.iospress.com/articles/journal-of-alzheimers-disease/jad230481</u>

BASIC DEMENTIA PROTOCOL IN A NUTSHELL

- 1) Find and correct/remove/re-balance any underlying causes that are contributing to the cognitive decline/dementia.
- 2) Diet Paleo/Mediterranean Ketogenic Diet with Time Restricted Eating
- 3) Exercise: 40 60 minutes a day (6 days/week)
- 4) Mindfulness/ Meditation/ Tai Chi or Chi Gung/ Guided Meditation/ HeartMath: 15+ minutes a day
- 5) Brain Training: Brain-HQ 15+ minutes a day
- 6) Sleep 8 hours a night, before midnight
- 7) Supplements as indicated by symptoms and testing to support processes affecting the brain and cognition
- 8) Optimize all Hormones

EVANTHEA DEMENTIA TRIAL – SUMMER 2023

- Randomized 9-month trial with 2/3 receiving Precision Medicine approach; 1/3 receiving standard of care Neurology treatment.
- 72 patients at 6 sites
- Standard of Care Neuro group will receive 6 months of active treatment at the conclusion of the 9-month trial, including coaching, supplements, testing, etc.
- Locations: Nashville, Cleveland, Hollywood Florida (north of Boca Raton/Miami), SF Marin County, SF – East Bay (Walnut Creek/Oakland), Sacramento
- Participants must live within 1 hour of a study location.

EVANTHEA DEMENTIA TRIAL

- Brain Biomarkers: p-Tau 217, NfL, GFAP
- Wearables: Oura Ring (for Sleep, HRV), and Continuous Glucose Monitors
- Home Mycotoxin testing before randomization
- Hearing and Vision testing if not done recently.
- Dental Cone Beam CT Scan if indicated (CBCT) with root canals or other issues.
- Optional HBOT, qEEG guided Neurofeedback, and Photobiomodulation available at several of the sites.
- http://DementiaReversalTrial.com/

DEMENTIA IS NOT A DEATH SENTENCE!

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HEARTMATH

www.HeartMath.com

BRAIN HQ BRAIN TRAINING

www.BrainHQ.com

CNSVS – CNS Vital Signs NeuroPsych Battery Online used to evaluate cognitive performance

https://www.cnsvs.com

MoCA – Montreal Cognitive Assessment Testing

https://mocacognition.com/

NeuroQuant – Volumetric MRI Testing

- https://Cortechs.ai
- Search for location near you that offer NeuroQuant scans.
- Reports to Order: Triage Brain Atrophy, Age-Related Atrophy, Multi-Structure Atrophy

Home Dust Testing for Mold/Mycotoxins

- www.LisBiotech.com Order ERMI dustcloth (includes HERTSMI scoring)
- Mycometrics.com Order ERMI dustcloth
- www.MyHouseMakesMeSick.com to score the Mycometrics testing for a Moldiness Index of your home. You upload the scores from Mycometrics testing to this program for a General Moldiness Index called a HERTSMI-2 score.

Nasal MARCoNS Infection Testing - MicrobiologyDx

https://microbiologydx.wixsite.com/dlmmicro

Lyme and Co-Infection Testing Companies

► Igenex

InfectoLab

► MDL

Home Dental Pathogen Testing

- My PerioPath (OralDNA.com)
- DirectDiagnostics.com
- Bristle Health
- SimplyPERIO

Testing Chemical Toxins and Heavy Metals

Real Time Labs EPP – Environmental Pollutants Panel (Chemical Toxins)

Great Plain Labs (Mosaics) Glyphosate (Roundup) level

Toxic metals testing – Whole Blood (Quest, LabCorp, Genova)

Micronutrient and Metals Testing

- Quest panels for: Antioxidants, B Vitamins, Minerals, and Heavy Metals
- LabCorp: Trace Minerals panel; Heavy Metals testing
- Genova NutrEval tests for all kinds of nutrient levels (including mitochondrial nutrients and omega fatty acid levels), some metal and chemical toxin levels, organic acids, and more.
- NutrEval covered by Medicare with appropriate diagnostic codes/indications

HOME SLEEP APNEA STUDY COMPANIES

Patient Safety, Inc

https://www.marketing.PatientSafetyInc.com/

WatchPAT One

https://www.itmar-medical.com/

PHOTOBIOMODULATION DEVICES

Auragen

https://reversalsolutions.com

https://reversalsolutions.com/pages/comparison-chart-1

Vielight

https://www.Vielight.com

GENERAL RESOURCES FOR MORE INFO

Precision Medicine Approach to Alzheimer's Disease: Successful Pilot Project – Kat Toups, Ann Hathaway, Deborah Gordon, Dale Bredesen, et al.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9484109/

ApoE4 Website by Julie Gregory – a Nutritionist with ApoE4 +/+ who healed with Dr. Bredesen's approach
 <u>ApoE4.info</u>

- Reversal of Cognitive Decline in Alzheimer's Disease Dale Bredesen, et al.
- https://pubmed.ncbi.nlm.nih.gov/27294343/
- Decoding Dementia free eBook Kat Toups, MD
- www.DementiaDemystified.com

► The End of Alzheimer's and other books by Dale Bredesen, MD

SOCIAL MEDIA INFO – ADDITIONAL DEMENTIA AND FUNCTIONAL PSYCHIATRY CONTENT

FACEBOOK PAGE: KAT TOUPS, MD - FUNCTIONAL MEDICINE PSYCHIATRY AND DEMENTIA <u>https://www.facebook.com/BayAreaWellness.net/</u> Lots of posts about the brain and neuroscience, including Dementia and Nutritional Psychiatry

► YOUTUBE CHANNEL – KAT TOUPS, MD

http://youtube.com/KatToupsMD Videos of talks on Dementia, as well as Functional Medicine Psychiatry topics

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