

New frontiers in the treatment and diagnosis of memory disorders

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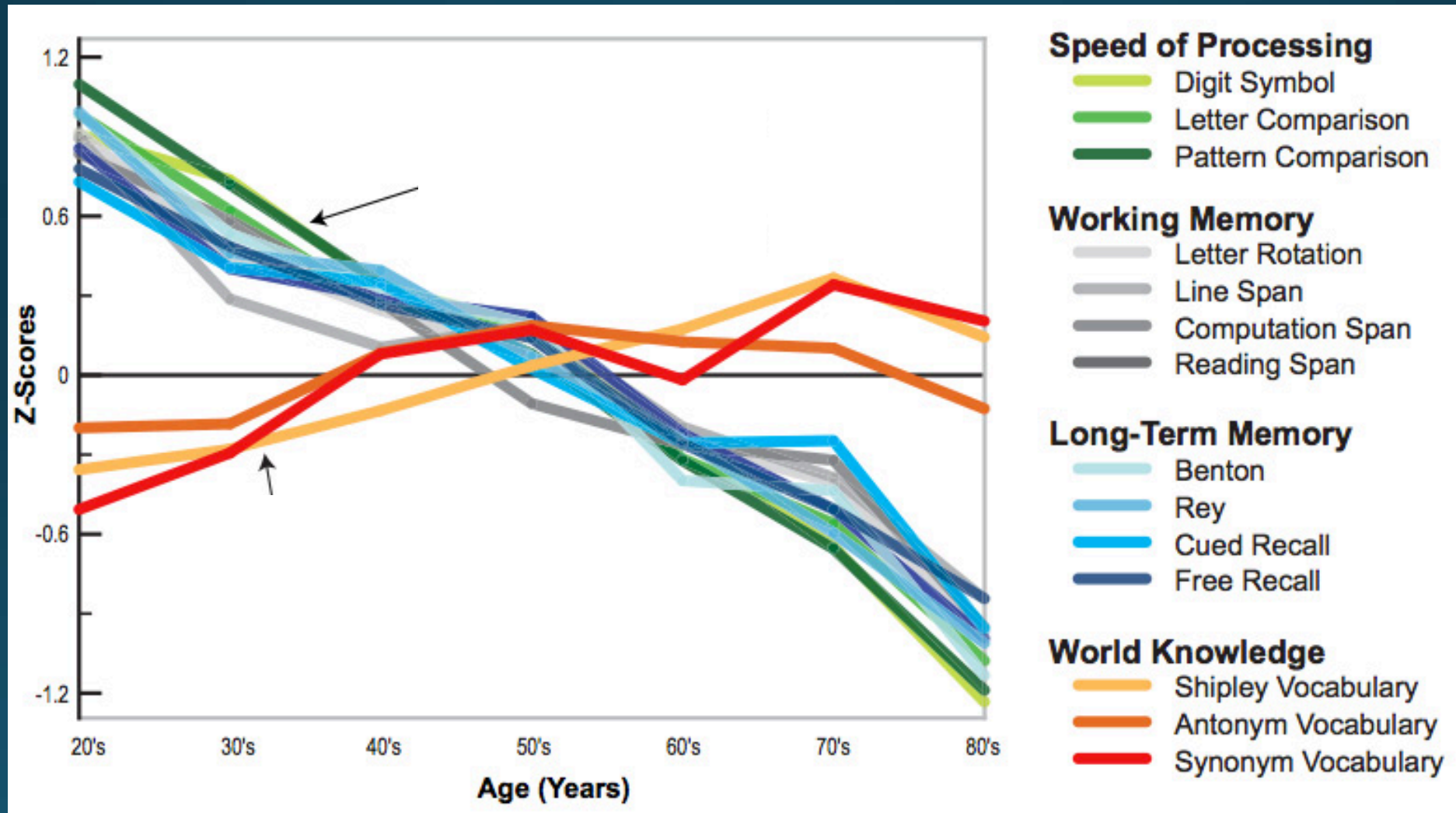
Saint Johns Medical Center

Legitimate hope for a dementia cure?

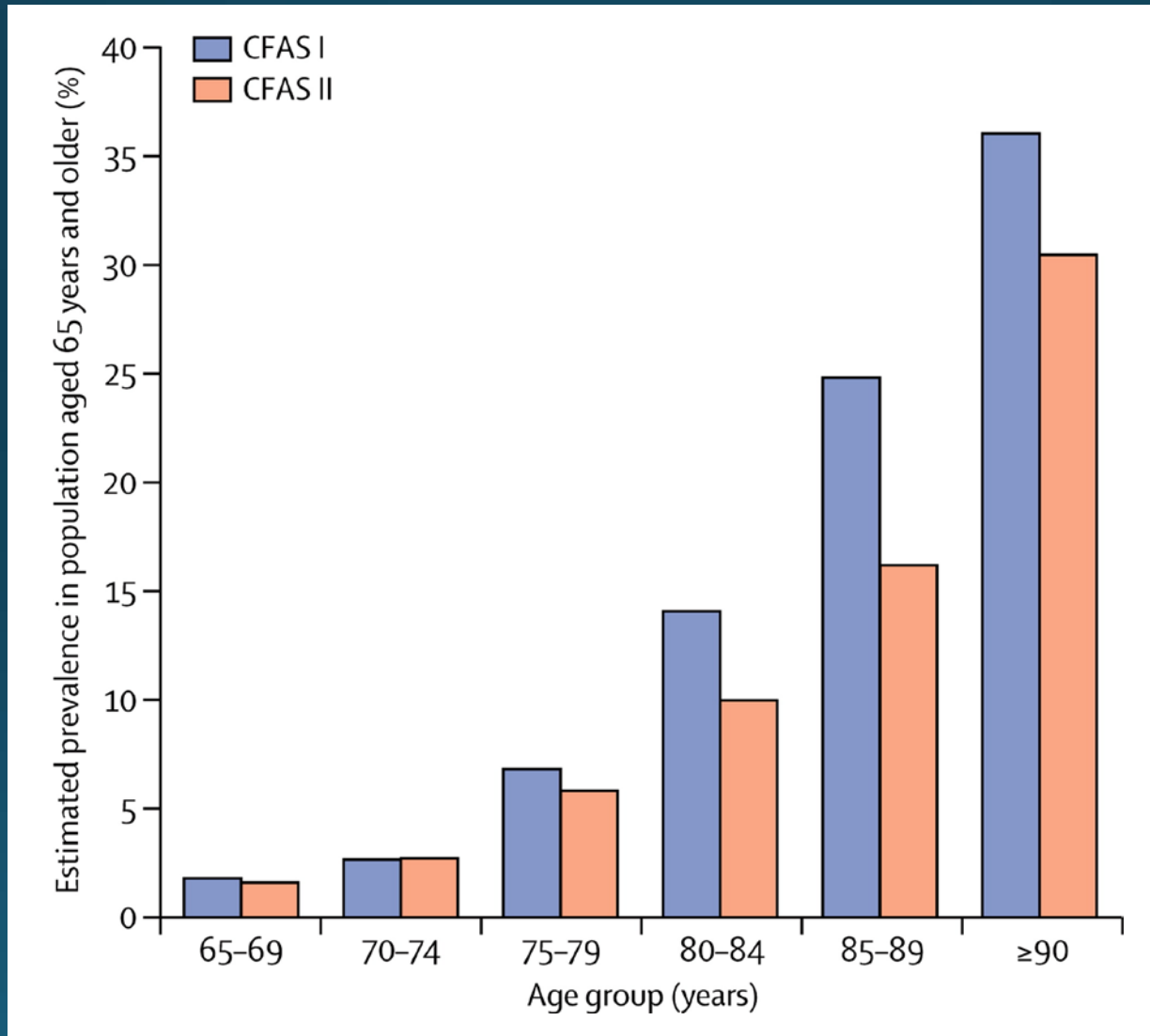


Advances in the diagnosis of memory loss and dementia

Raw memory declines with age



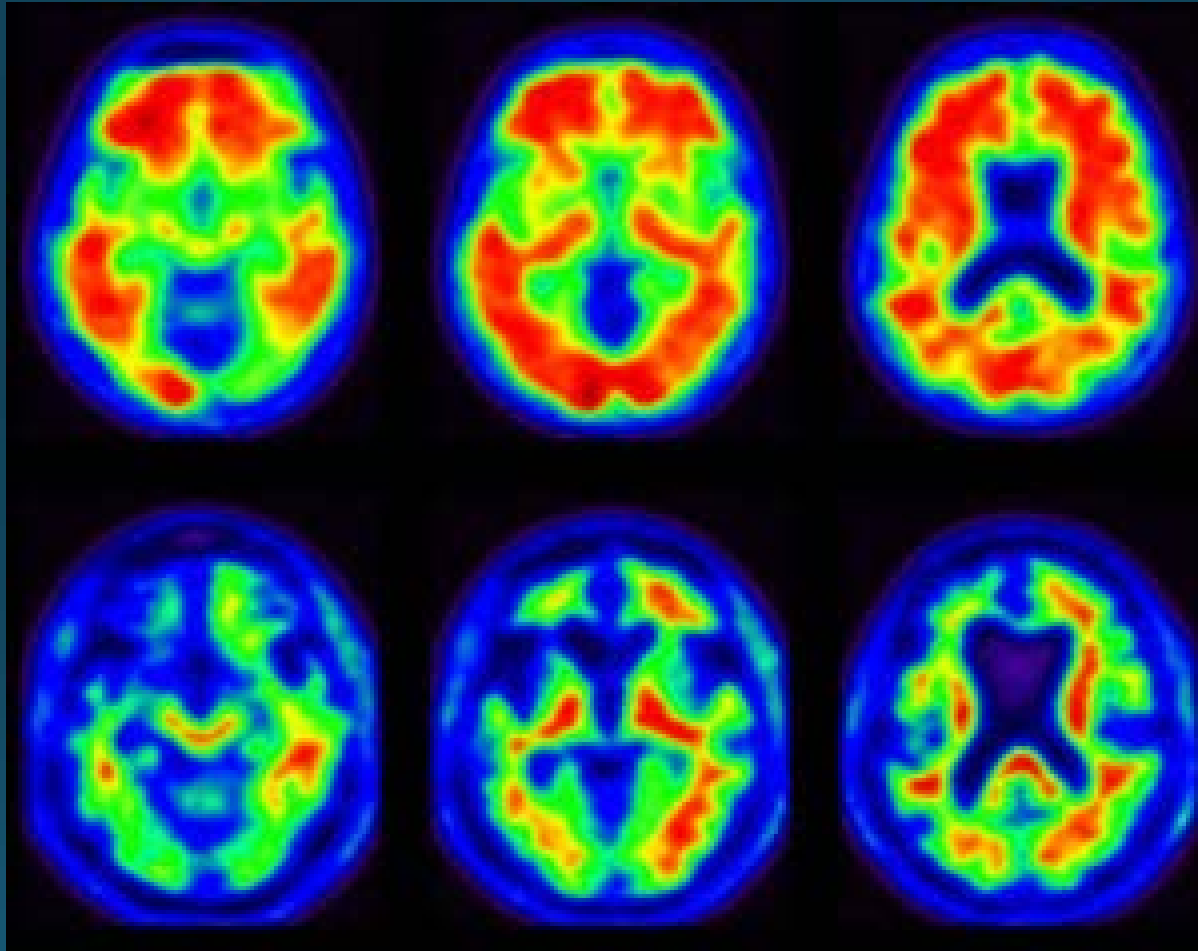
Dementia prevalence dramatically increases with age



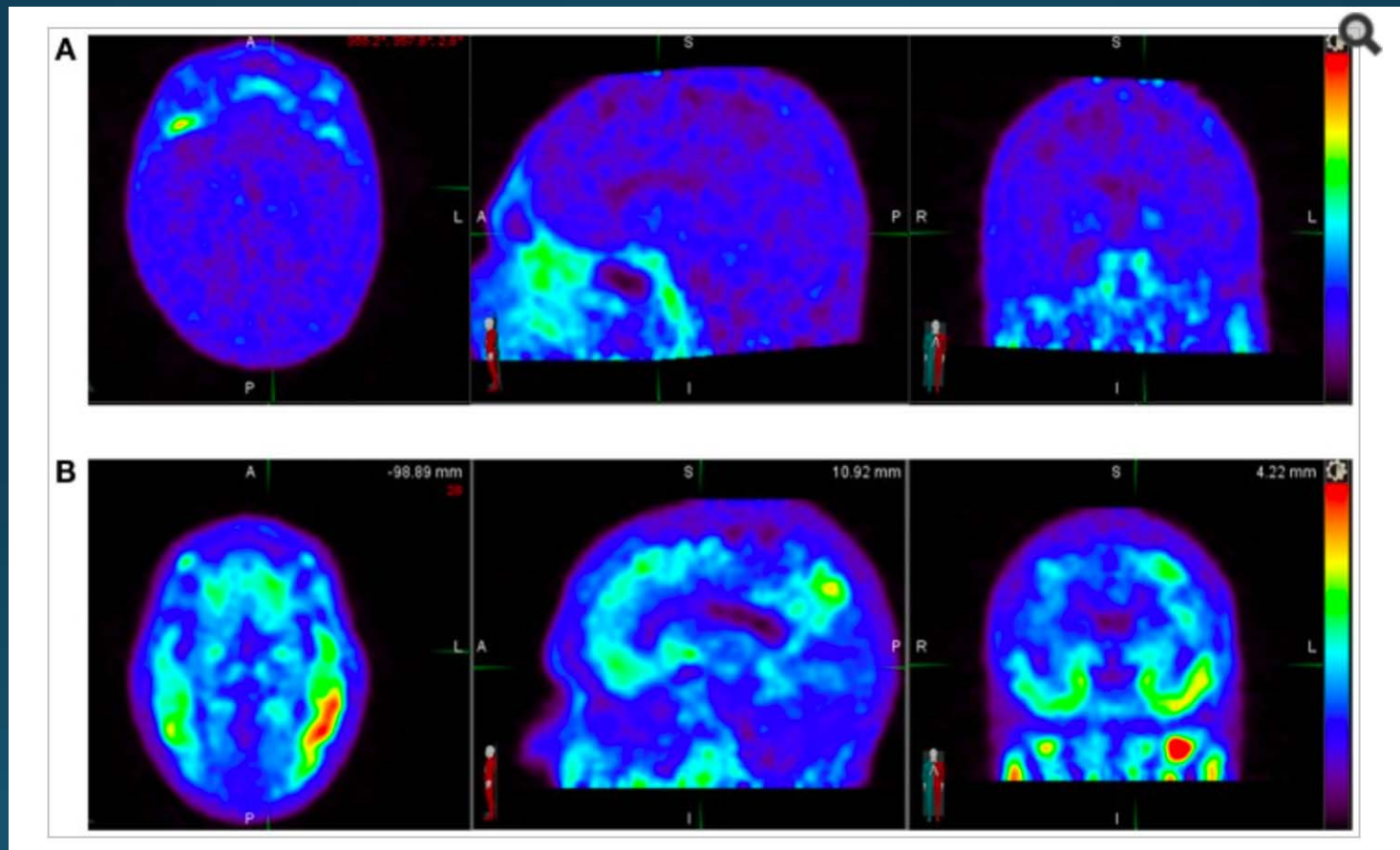
Diagnostic challenges in memory loss

- Normal memory loss in aging
- Depression
- Medication side effects
- Depression
- COPD and insomnia
- Hypertensive disease
- Alcohol abuse (or other substances -- marijuana, opium)
- Late onset neuroinflammatory disease/ multiple sclerosis
- Normal pressure hydrocephalus
- B₁₂, Thiamine deficiency
- Vasculitis, HIV, hypothyroidism, tumor, adrenal insufficiency ...

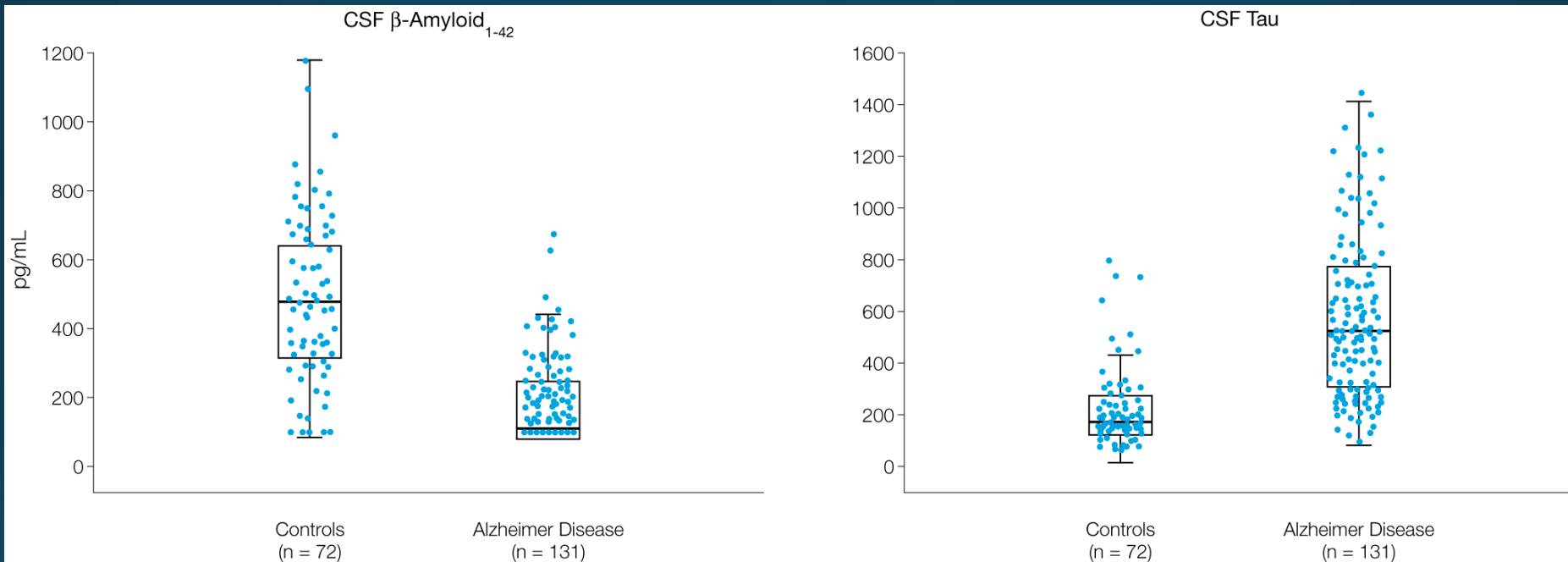
IDEAS



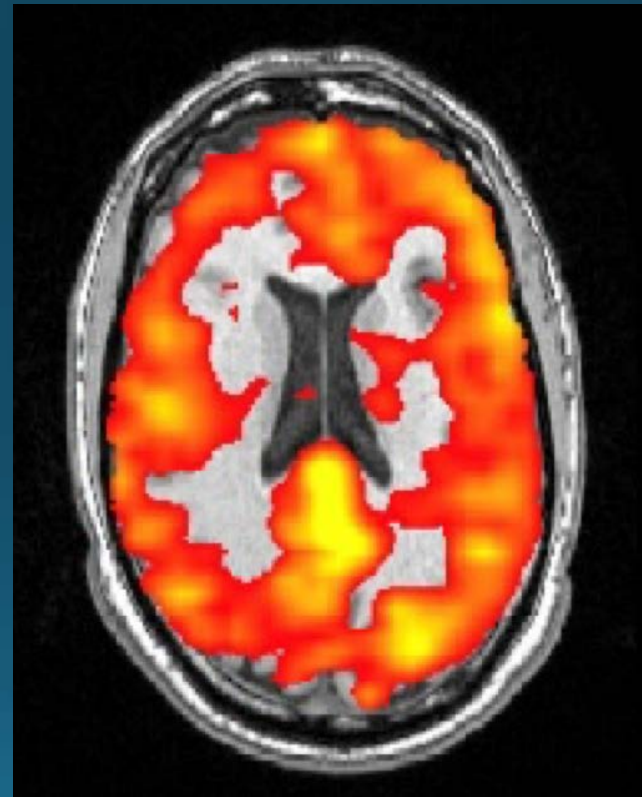
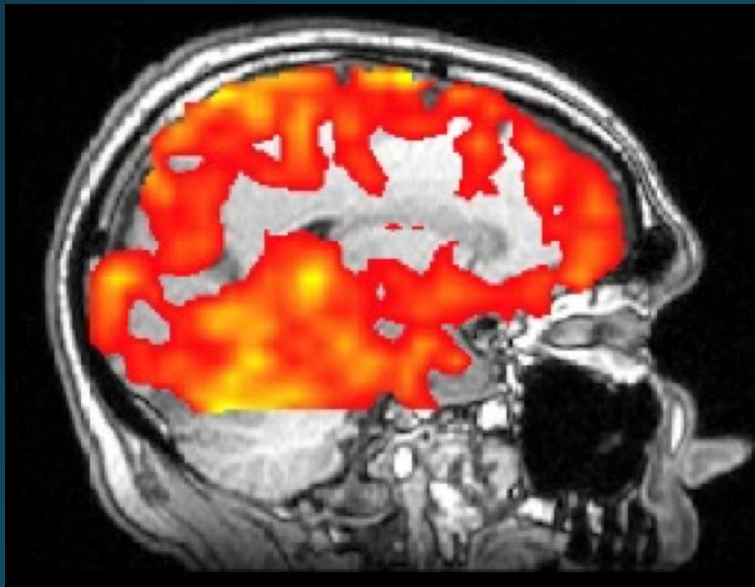
Tau scan



CSF analysis

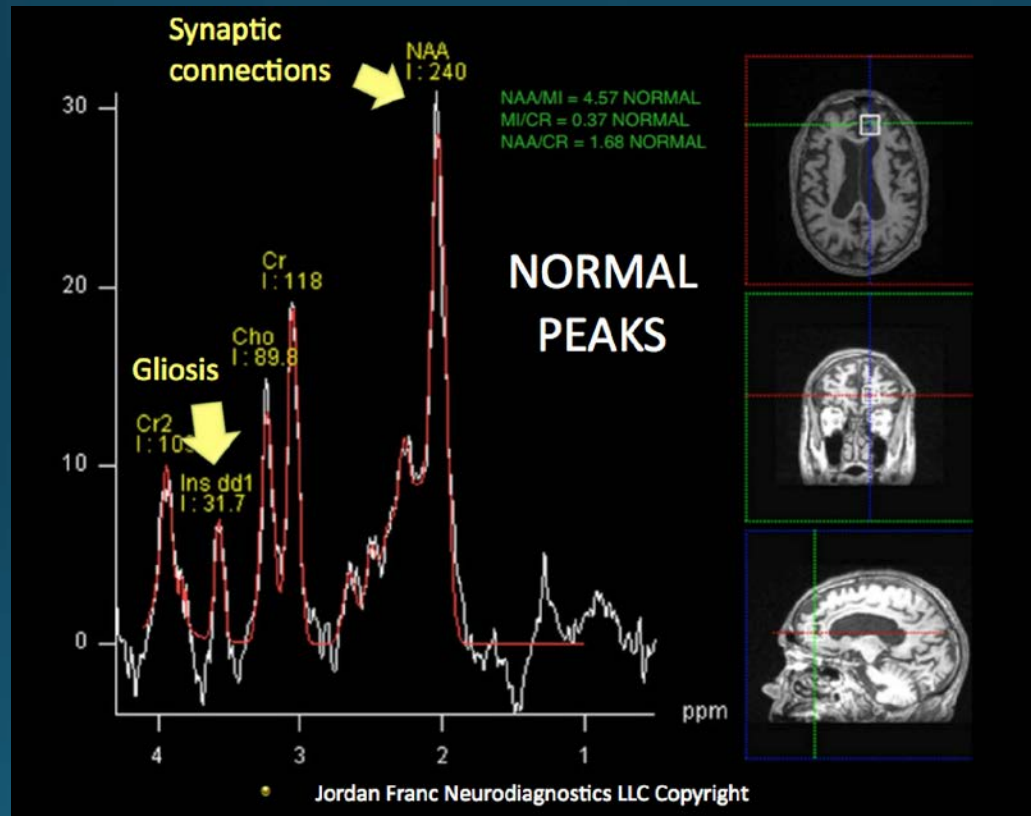


Advanced MRI for neurodegenerative disease diagnosis – normal



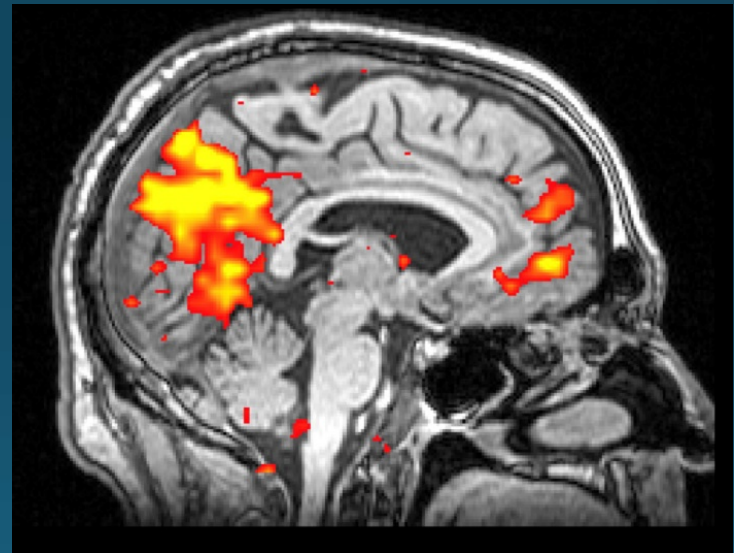
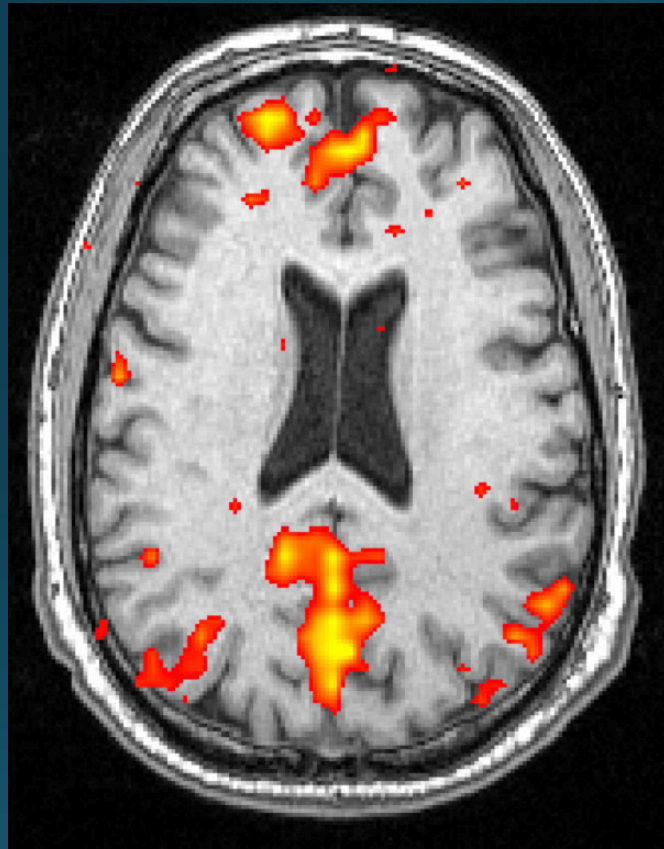
Courtesy Dr. Sheldon Jordan

Advanced MRI for neurodegenerative disease diagnosis – normal



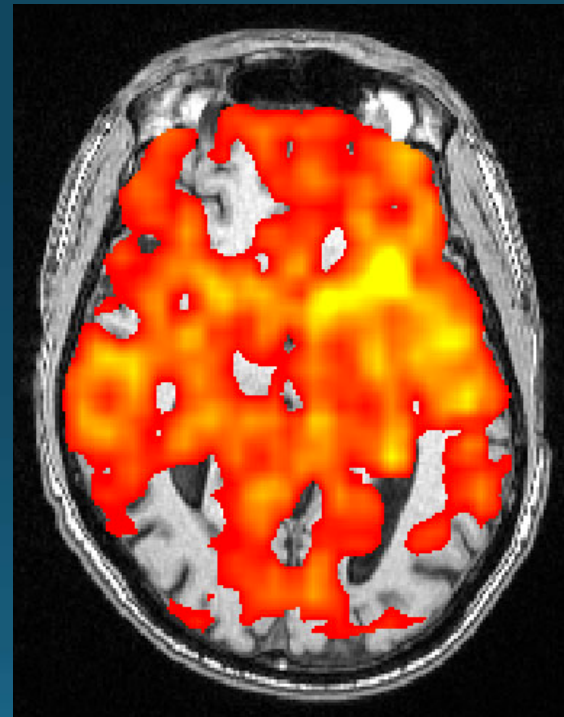
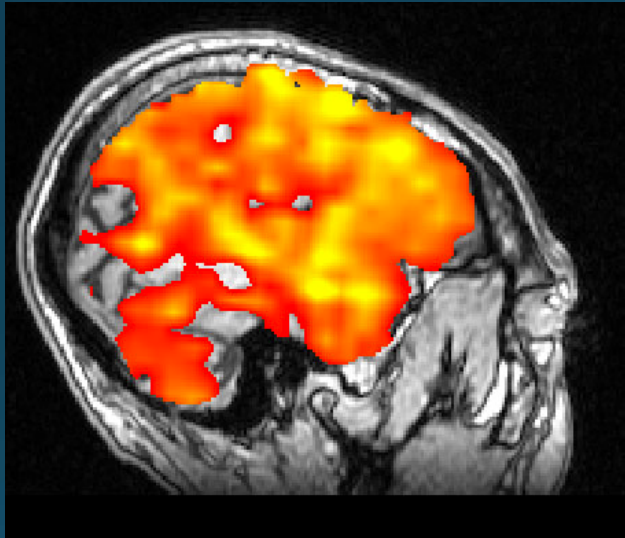
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Advanced MRI for neurodegenerative disease diagnosis – normal



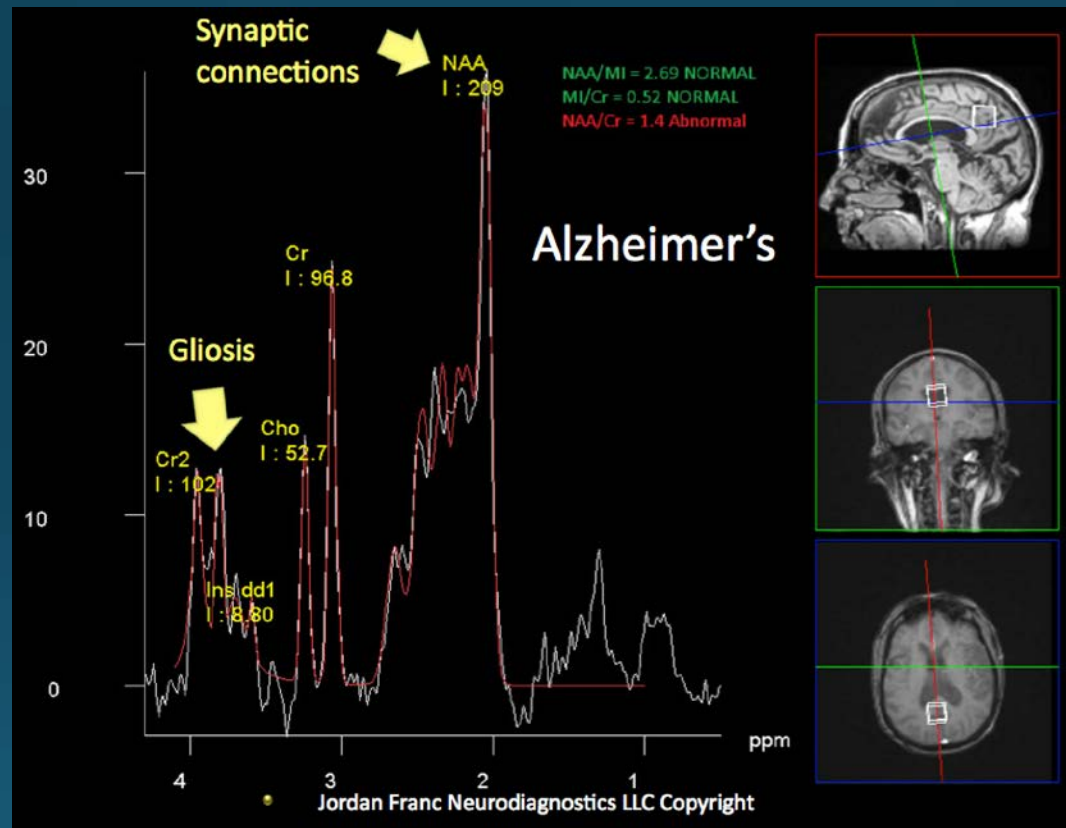
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Advanced MRI for neurodegenerative disease diagnosis – Alzheimer's diagnosis



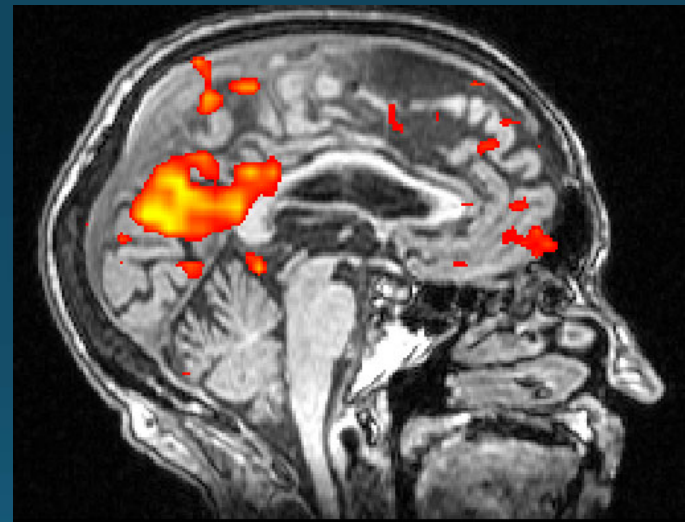
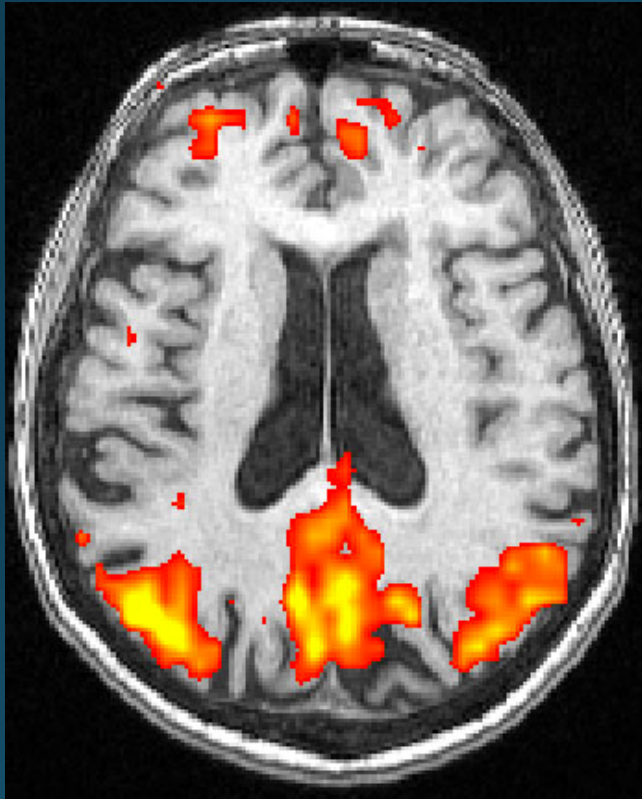
Courtesy Dr. Sheldon Jordan

Advanced MRI for neurodegenerative disease diagnosis – Alzheimer's diagnosis



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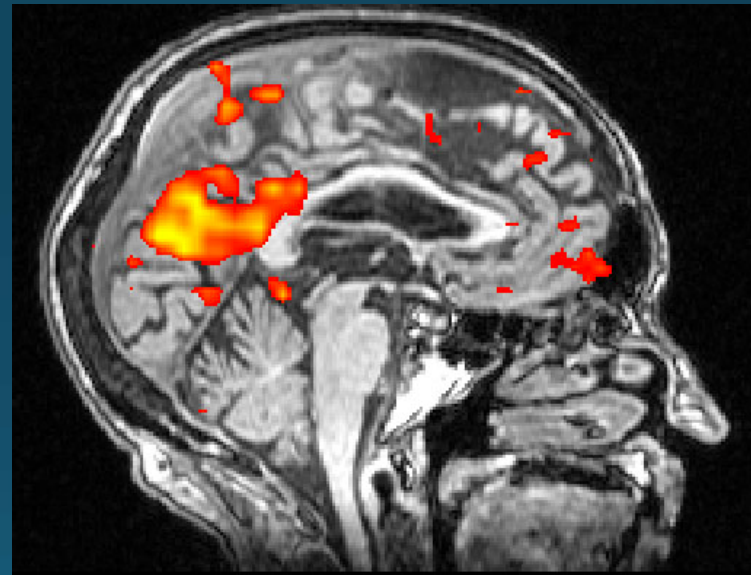
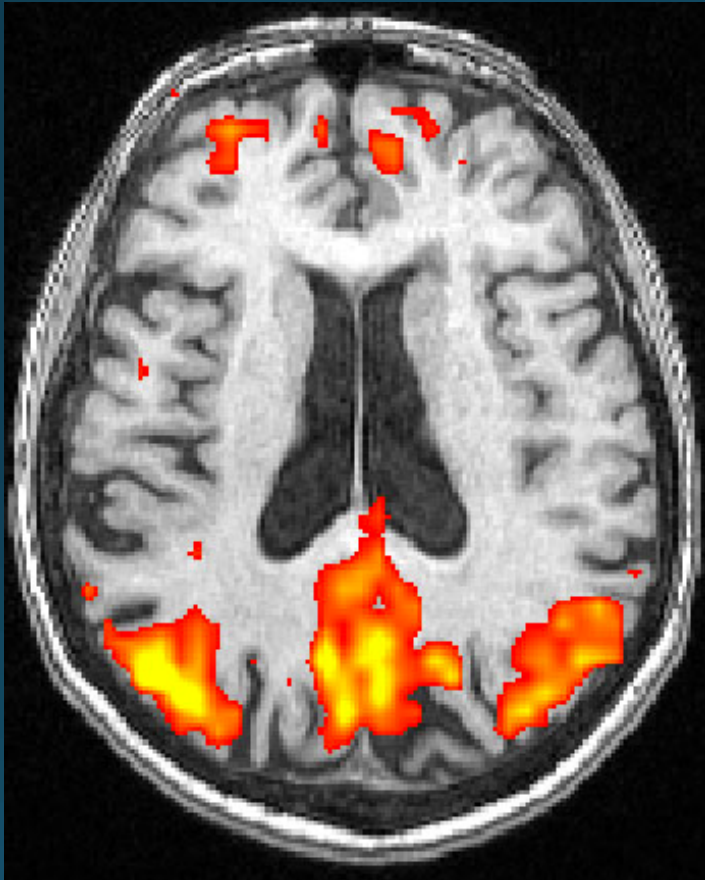
Advanced MRI for neurodegenerative disease diagnosis – Alzheimer's diagnosis



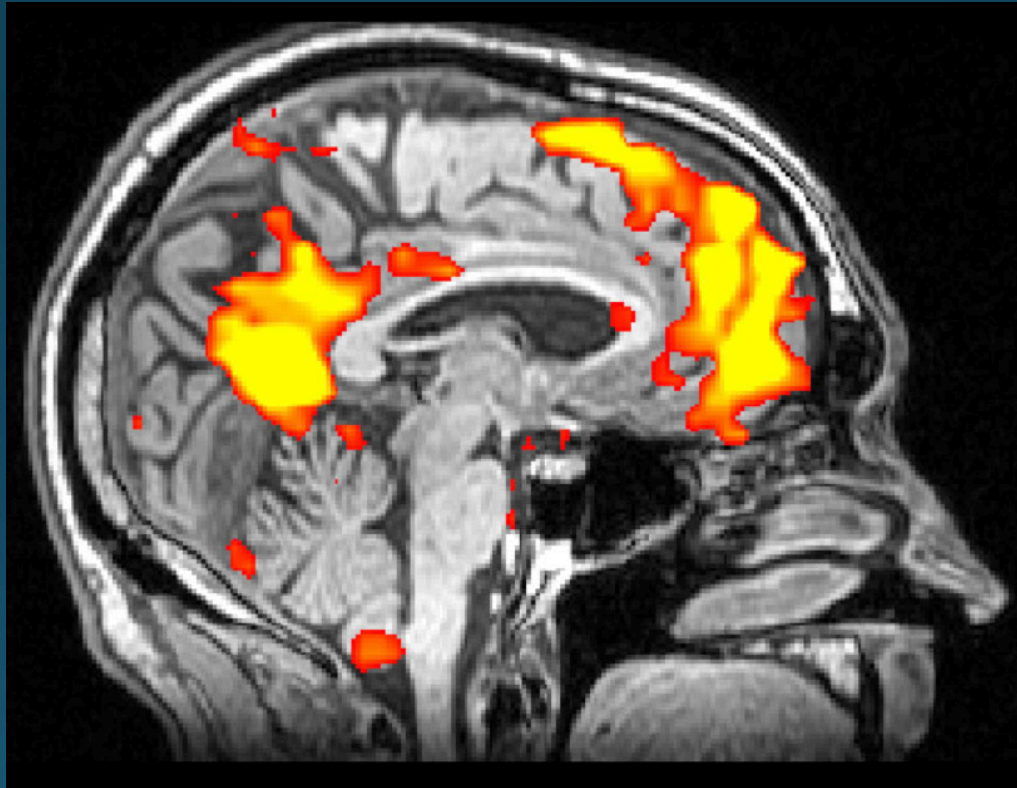
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BOLD ICA

Frontal Temporal Dementia Default Network

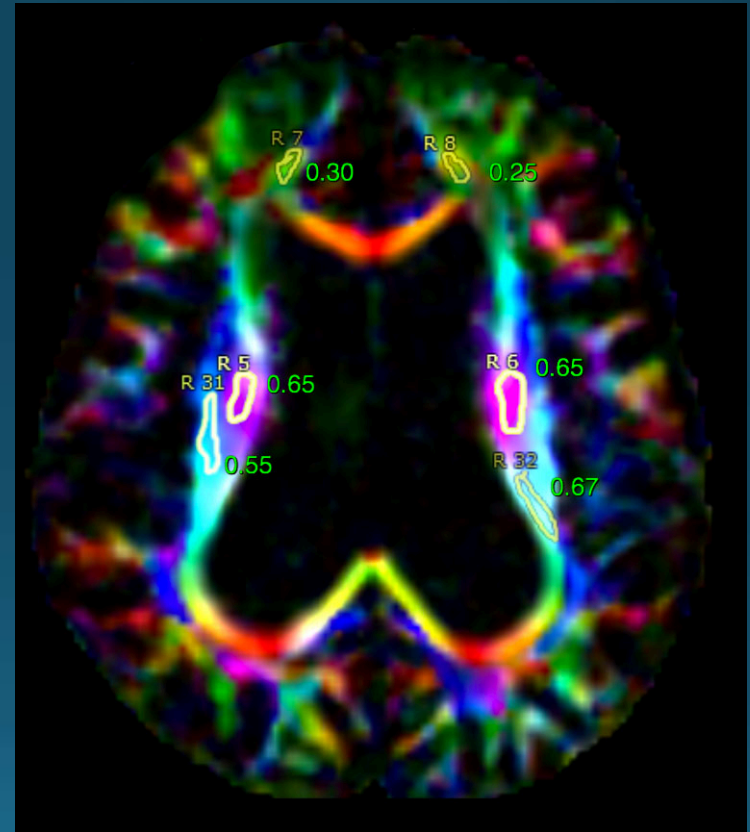
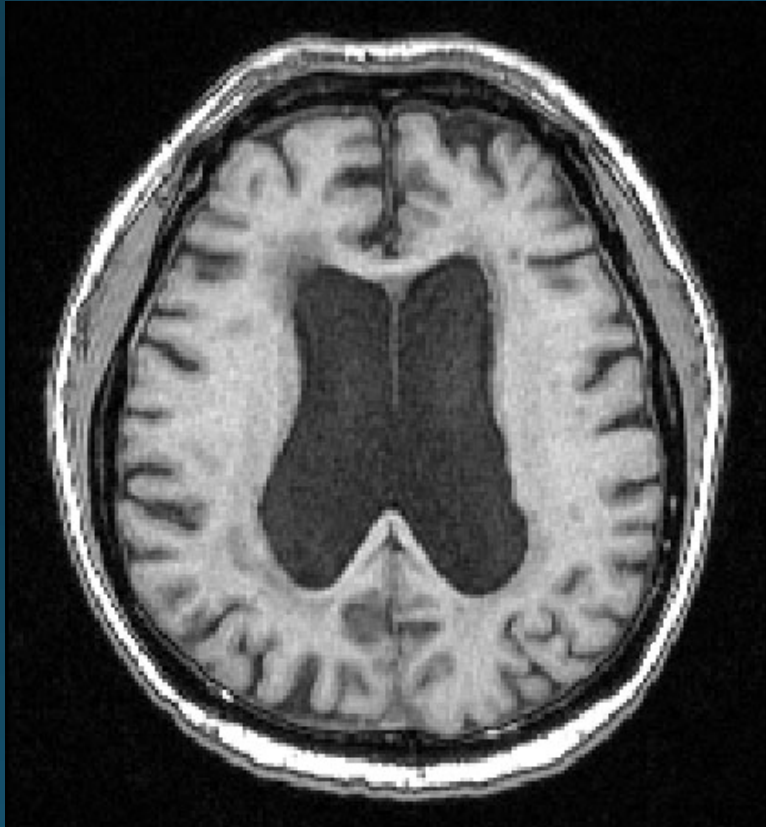


BOLD ICA Default Network – Anxiety Disorder



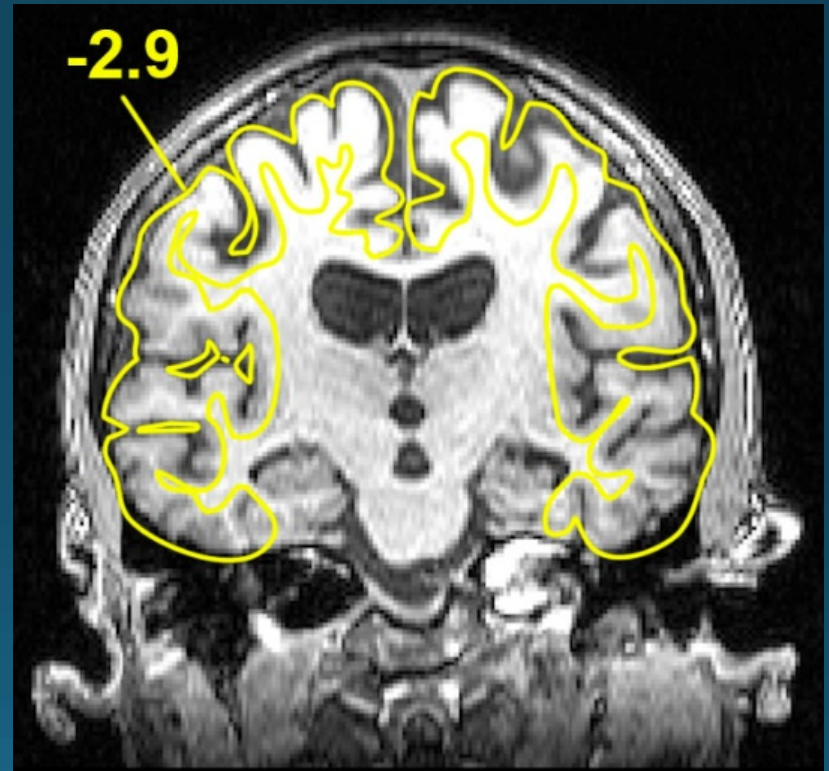
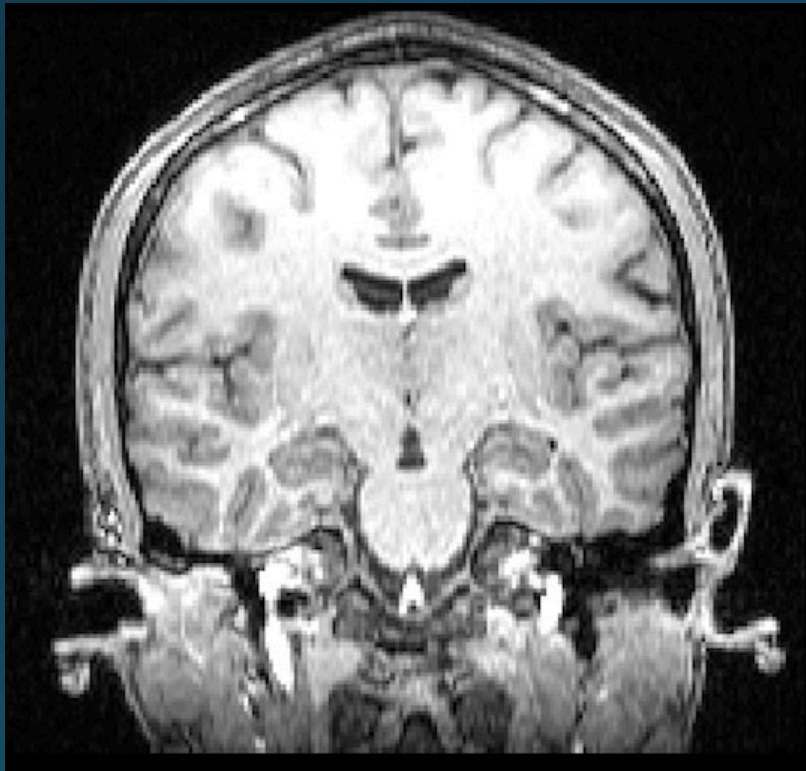
Courtesy Dr. Sheldon Jordan

Advanced neuroimaging: diffusion tensor imaging



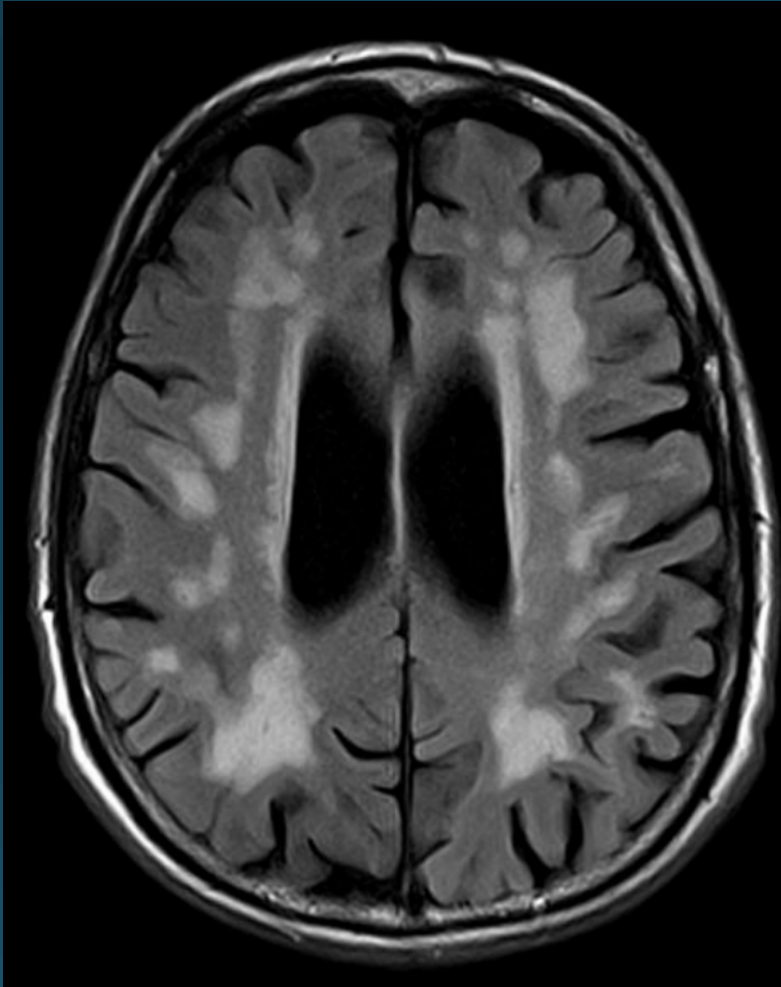
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Advanced neuroimaging: quantitative volumetric analysis



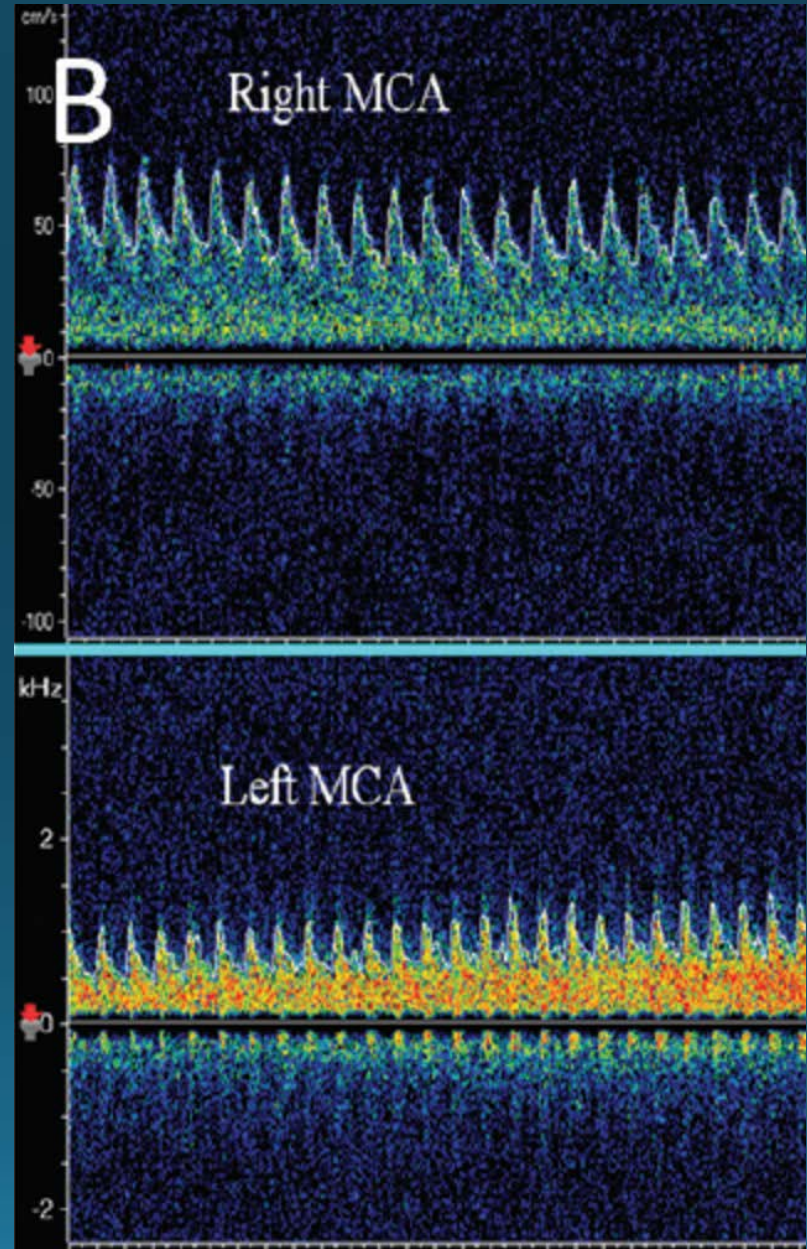
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White matter disease/cardiovascular



- Elevated risk of Alzheimer's with history of hypertension, white matter disease, intracranial atherosclerosis

TCD measures of vasomotor reactivity

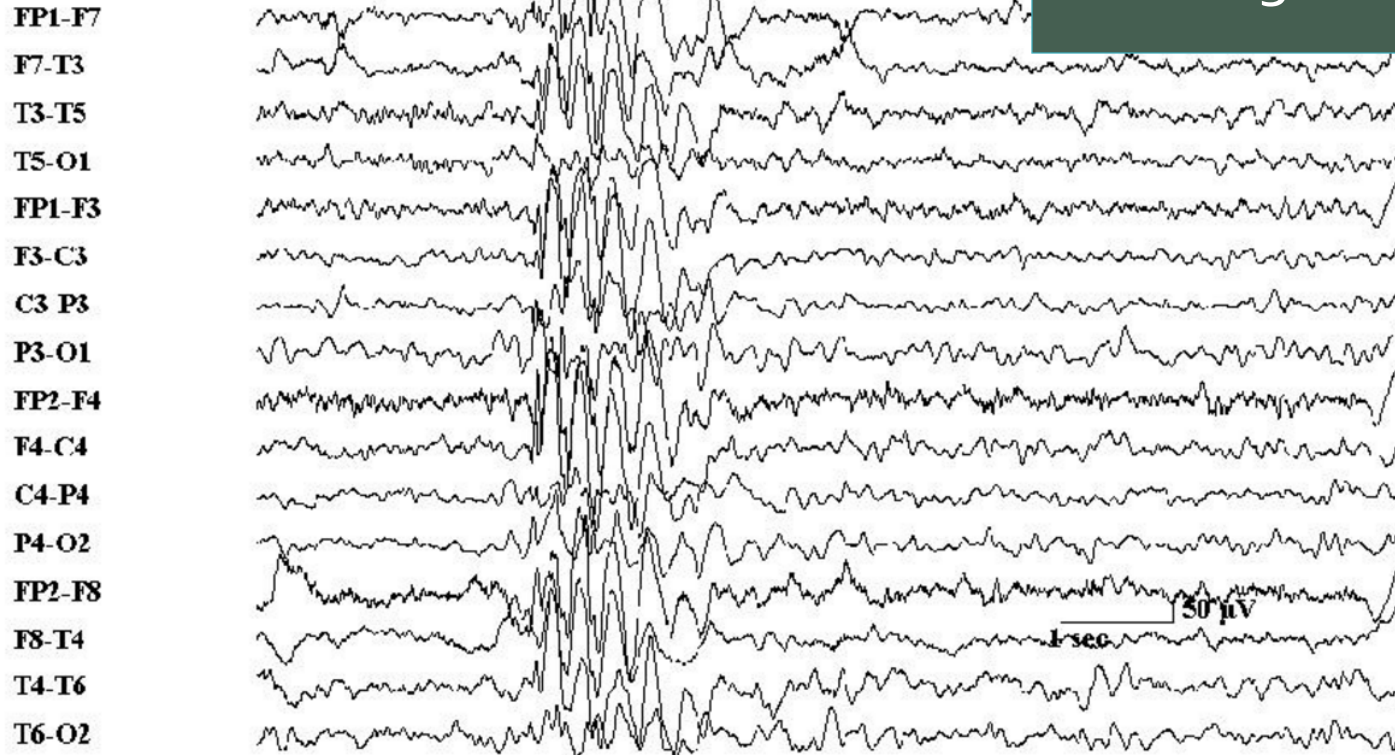


Advanced MRI measures of vasomotor reactivity

Courtesy Dr. Sheldon Jordan

Initial memory loss evaluation: seizures

Evaluate for epileptiform
discharges



Advances in the treatment of memory loss and dementia

Dementia therapy trial: nilotinib

CANCER DRUG IMPROVED COGNITION AND MOTOR SKILLS IN SMALL PARKINSON'S CLINICAL TRIAL

CHICAGO (Oct. 17, 2015) — An FDA-approved drug for leukemia improved cognition, motor skills and non-motor function in patients with Parkinson's disease and Lewy body dementia in a small phase I clinical trial, report researchers at Georgetown University Medical Center (GUMC) in Washington. In addition, the drug, nilotinib (Tasigna® by Novartis), led to statistically significant and encouraging changes in toxic proteins linked to disease progression (biomarkers).

Complete data were presented at Neuroscience 2015, the annual meeting of the Society for Neuroscience, in Chicago on Oct. 17.

Charbel Moussa, MD, PhD, who directs Georgetown's Laboratory of Dementia and Parkinsonism, conducted the preclinical research that led to the discovery of nilotinib for the treatment of neurodegenerative diseases. To conduct the clinical study, he partnered with Fernando Pagan, MD, a GUMC associate professor of neurology who directs the Movement Disorders Program at MedStar Georgetown University Hospital.



Charbel Moussa, MD, PhD

MEDIA ONLY:

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PATIENT INFORMATION: Parkinson's disease/Lewy body dementia

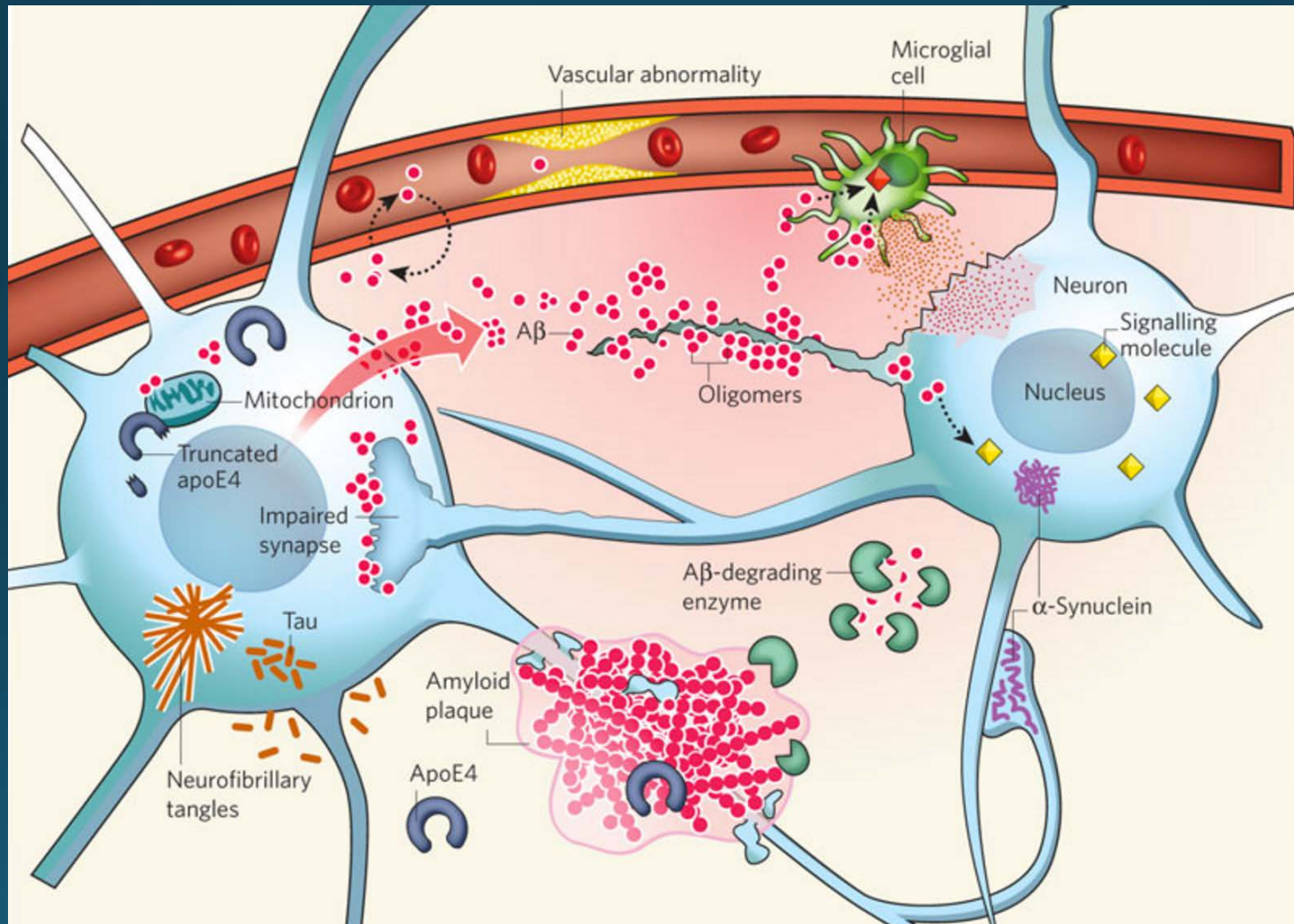
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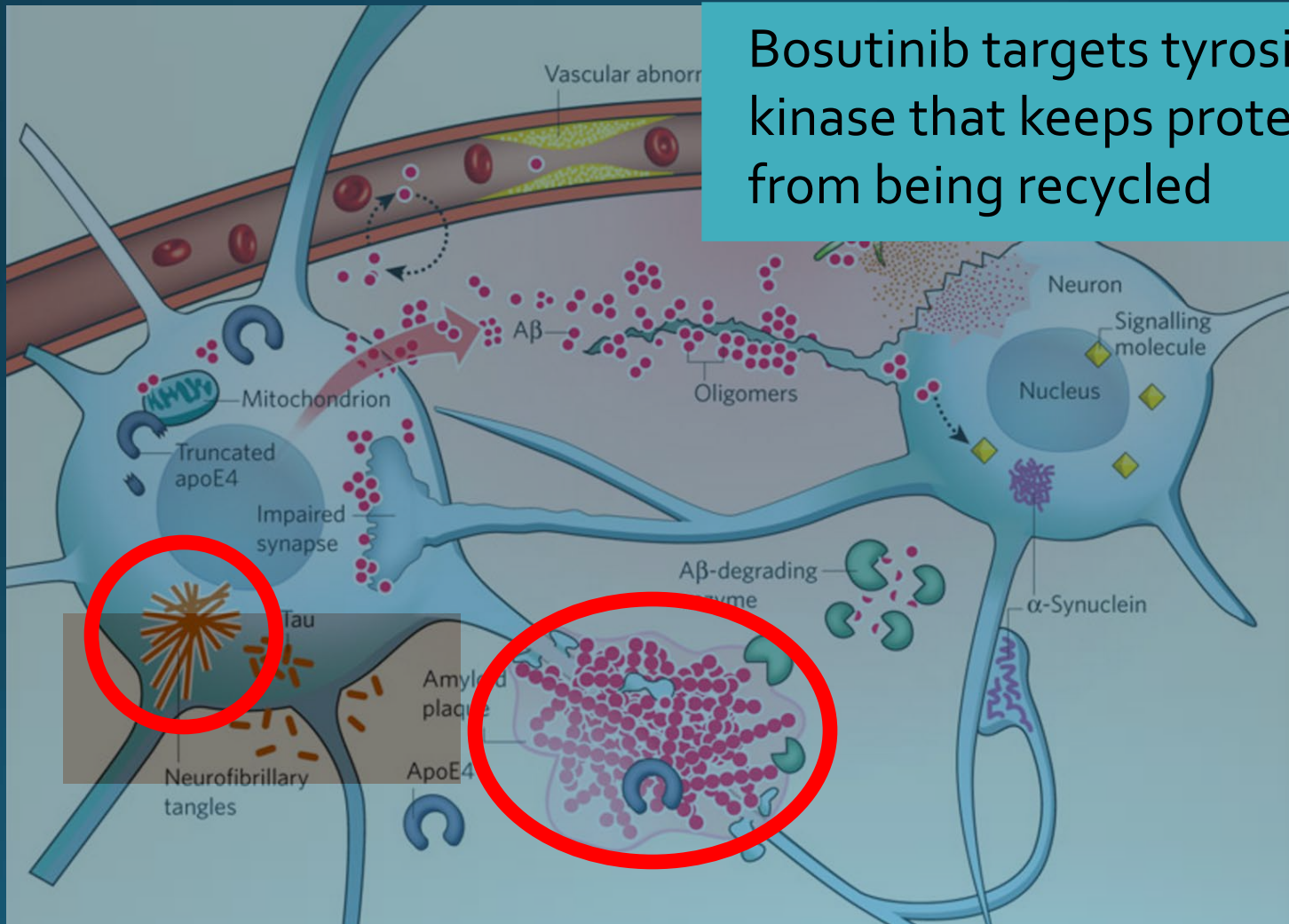
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Dementia new therapy: bosutinib



Dementia new therapy: bosutinib

Bosutinib targets tyrosine kinase that keeps proteins from being recycled



Dementia new therapy: tyrosine kinase inhibitors

Announcements

NEW CLINICAL TRIAL WILL TEST CANCER DRUG AS ALZHEIMER'S TREATMENT

The Alzheimer's Drug Discovery Foundation (ADDF) announces a \$2.1 million grant awarded to R. Scott Turner, MD, PhD, of Georgetown University Medical Center to conduct a phase II clinical trial of low-dose nilotinib (marketed as Tasigna® for use as a cancer therapy) in patients with Alzheimer's disease.



Dementia therapy trial: nilotinib

- Ongoing Phase 1+ boisutinib trial
 - In conjunction with Dr. Sheldon Jordan, Dr. Santosh Kesari and other Saint Johns physicians
 - Ongoing trial of 20 opatients patients with mild, moderate, and severe dementia including Alzheimer's and frontotemporal dementiaMRI, spinal fluid and neurocognitive testing
 - Will follow memory and MRI scores
- Plan for Phase 3-4 clinical trial

Focused ultrasound for treatment of Alzheimer's dementia

RESEARCH ARTICLE

ALZHEIMER'S DISEASE

Scanning ultrasound removes amyloid- β and restores memory in an Alzheimer's disease mouse model

Gerhard Leinenga and Jürgen Götz*

Amyloid- β (A β) peptide has been implicated in the pathogenesis of Alzheimer's disease (AD). We present a non-pharmacological approach for removing A β and restoring memory function in a mouse model of AD in which A β is deposited in the brain. We used repeated scanning ultrasound (SUS) treatments of the mouse brain to remove A β , without the need for any additional therapeutic agent such as anti-A β antibody. Spinning disk confocal microscopy and high-resolution three-dimensional reconstruction revealed extensive internalization of A β into the lysosomes of activated microglia in mouse brains subjected to SUS, with no concomitant increase observed in the number of microglia. Plaque burden was reduced in SUS-treated AD mice compared to sham-treated animals, and cleared plaques were observed in 75% of SUS-treated mice. Treated AD mice also displayed improved performance on three memory tasks: the Y-maze, the novel object recognition test, and the active place avoidance task. Our findings suggest that repeated SUS is useful for removing A β in the mouse brain without causing overt damage, and should be explored further as a noninvasive method with therapeutic potential in AD.

Focused ultrasound for treatment of Alzheimer's dementia

- Ongoing Phase 1+ trial
 - In conjunction with Dr. Sheldon Jordan, Dr. Santosh Kesari and other Saint Johns physicians
 - Ongoing trial of 20 patients with mild, moderate, and severe dementia including Alzheimer's and frontotemporal dementia MRI, spinal fluid and neurocognitive testing
 - Will follow memory and MRI scores
- Future focused ultrasound trials with Pacific Neuroscience and Saint Johns Medical Center

Dementia therapy trial: transcranial magnetic stimulation

TMS can be used to stimulate brain networks affected by Alzheimer's dementia



Dementia therapy trial: transcranial magnetic stimulation

- Empiric treatment of memory loss in patients with diagnosed neurodegenerative disease
 - MRI, spinal fluid, neurocognitive testing
 - EEG to assess for seizures or discharges
 - 12-18 month follow up
- Please contact if interested in more information

Dementia treatment: holistic approach

www.impactaging.com

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Review

Reversal of cognitive decline: A novel therapeutic program

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Key words: Alzheimer's, dementia, mild cognitive impairment, neurobehavioral disorders, neuroinflammation, neurodegeneration, systems biology

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Abstract: This report describes a novel, comprehensive, and personalized therapeutic program that is based on the underlying pathogenesis of Alzheimer's disease, and which involves multiple modalities designed to achieve metabolic enhancement for neurodegeneration (MEND). The first 10 patients who have utilized this program include patients with memory loss associated with Alzheimer's disease (AD), amnesic mild cognitive impairment (aMCI), or subjective cognitive impairment (SCI). Nine of the 10 displayed subjective or objective improvement in cognition beginning within 3-6 months, with the one failure being a patient with very late stage AD. Six of the patients had had to discontinue working or were struggling with their jobs at the time of presentation, and all were able to return to work or continue working with improved performance. Improvements have been sustained, and at this time the longest patient follow-up is two and one-half years from initial treatment, with sustained and marked improvement. These results suggest that a larger, more extensive trial of this therapeutic program is warranted. The results also suggest that, at least early in the course, cognitive decline may be driven in large part by metabolic processes. Furthermore, given the failure of monotherapeutics in AD to date, the results raise the possibility that such a therapeutic system may be useful as a platform on which drugs that would fail as monotherapeutics may succeed as key components of a therapeutic system.

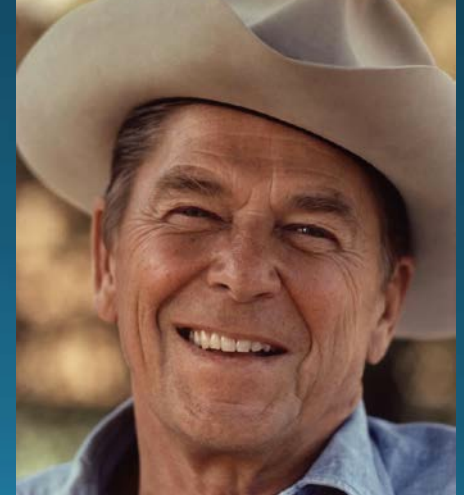
Dementia treatment: holistic approach

Table 1. Therapeutic System 1.0

Goal	Approach	Rationale and References
Optimize diet: minimize simple CHO, minimize inflammation.	Patients given choice of several low glycemic, low inflammatory, low grain diets.	Minimize inflammation, minimize insulin resistance.
Enhance autophagy, ketogenesis	Fast 12 hr each night, including 3 hr prior to bedtime.	Reduce insulin levels, reduce A β .
Reduce stress	Personalized—yoga or meditation or music, etc.	Reduction of cortisol, CRF, stress axis.
Optimize sleep	8 hr sleep per night; melatonin 0.5mg po qhs; Trp 500mg po 3x/wk if awakening. Exclude sleep apnea.	[36]
Exercise	30-60' per day, 4-6 days/wk	[37, 38]
Brain stimulation	Posit or related	[39]
Homocysteine <7	Me-B12, MTHF, P5P; TMG if necessary	[40]
Serum B12 >500	Me-B12	[41]
CRP <1.0; A/G >1.5	Anti-inflammatory diet; curcumin; DHA/EPA; optimize hygiene	Critical role of inflammation in AD
Fasting insulin <7; HgbA1c <5.5	Diet as above	Type II diabetes-AD relationship
Hormone balance	Optimize fT3, fT4, E2, T, progesterone, pregnenolone, cortisol	[5, 42]
GI health	Repair if needed; prebiotics and probiotics	Avoid inflammation, autoimmunity
Reduction of A-beta	Curcumin, Ashwagandha	[43-45]
Cognitive enhancement	Bacopa monniera, MgT	[46, 47]
25OH-D3 = 50-100ng/ml	Vitamins D3, K2	[48]
Increase NGF	H. erinaceus or ALCAR	[49, 50]
Provide synaptic structural components	Citicoline, DHA	[51].
Optimize antioxidants	Mixed tocopherols and tocotrienols, Se, blueberries, NAC, ascorbate, α -lipoic acid	[52]
Optimize Zn:fCu ratio	Depends on values obtained	[53]
Ensure nocturnal oxygenation	Exclude or treat sleep apnea	[54]
Optimize mitochondrial function	CoQ or ubiquinol, α -lipoic acid, PQQ, NAC, ALCAR, Se, Zn, resveratrol, ascorbate,	[55]

- Improve sleep
- Treat stress and anxiety
- Regular exercise
- Improve diet
- Cognitive exercises
- Supplements
 - Coconut oil, MCT oil
 - Curcumin
 - Resveratrol

- Beyond Alzheimer's patient support group founded by Patti Davis moving to Saint Johns Medical Center in May 2016
 - Support for family members of patients with Alzheimers and other neurodegenerative diseases
- Please contact if interested in more information



Thanks for your interest!

