

*ADC Spring Meeting 2015
Clinical Core Leaders Meeting
April 18, 2015 , Washington, DC*

What should we do until we have a prevention for AD?

Practices and Investigational Approaches to Symptom Management

Steven E. Arnold, M.D., Introduction



Martin R. Farlow, MD: Pharmacological Approaches for Cognition



Laura D. Baker, PhD: Exercise and Non-Pharmacological Approaches



Constantine G. Lyketsos, MD: MIND & Community Dementia Care



Murray A. Raskind, MD: Prazosin for Agitation & Drug Re-Purposing

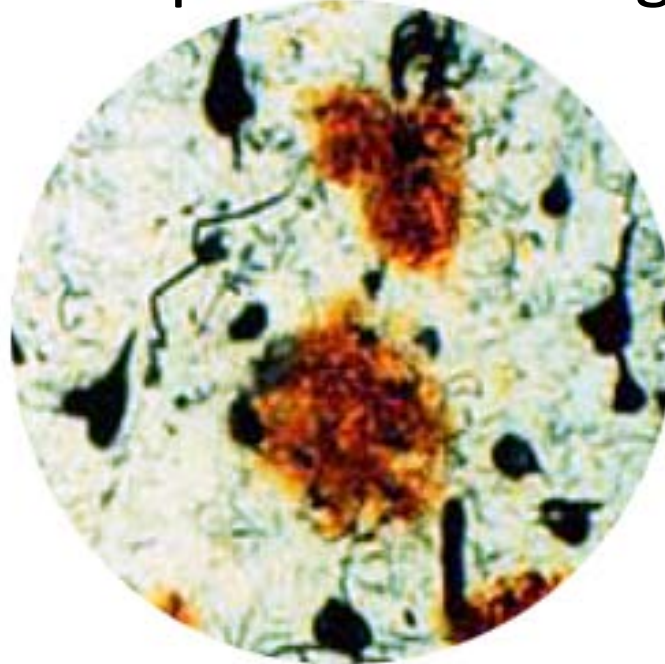


Alzheimer's Disease

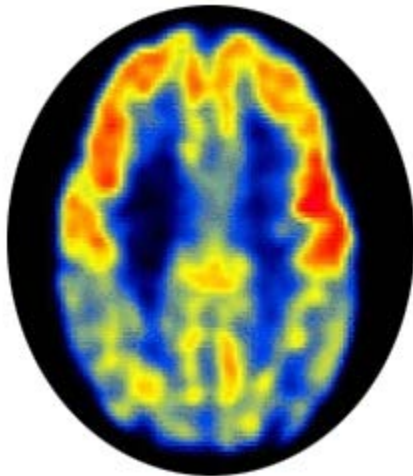
A β Plaques & Tau Tangles

CSF Amyloid & Tau

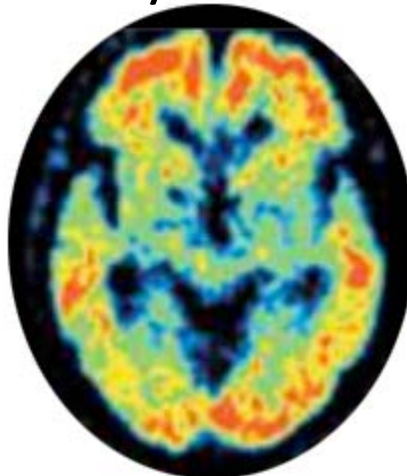
MRI Volumetry



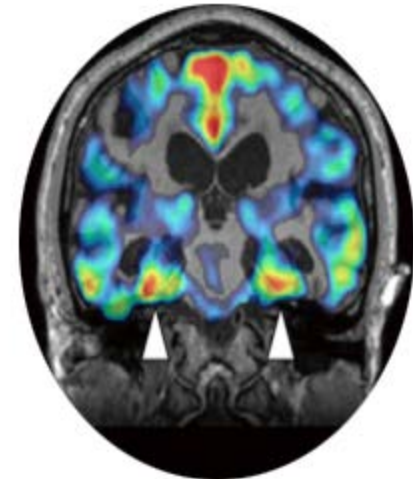
FDG PET



Amyloid PET

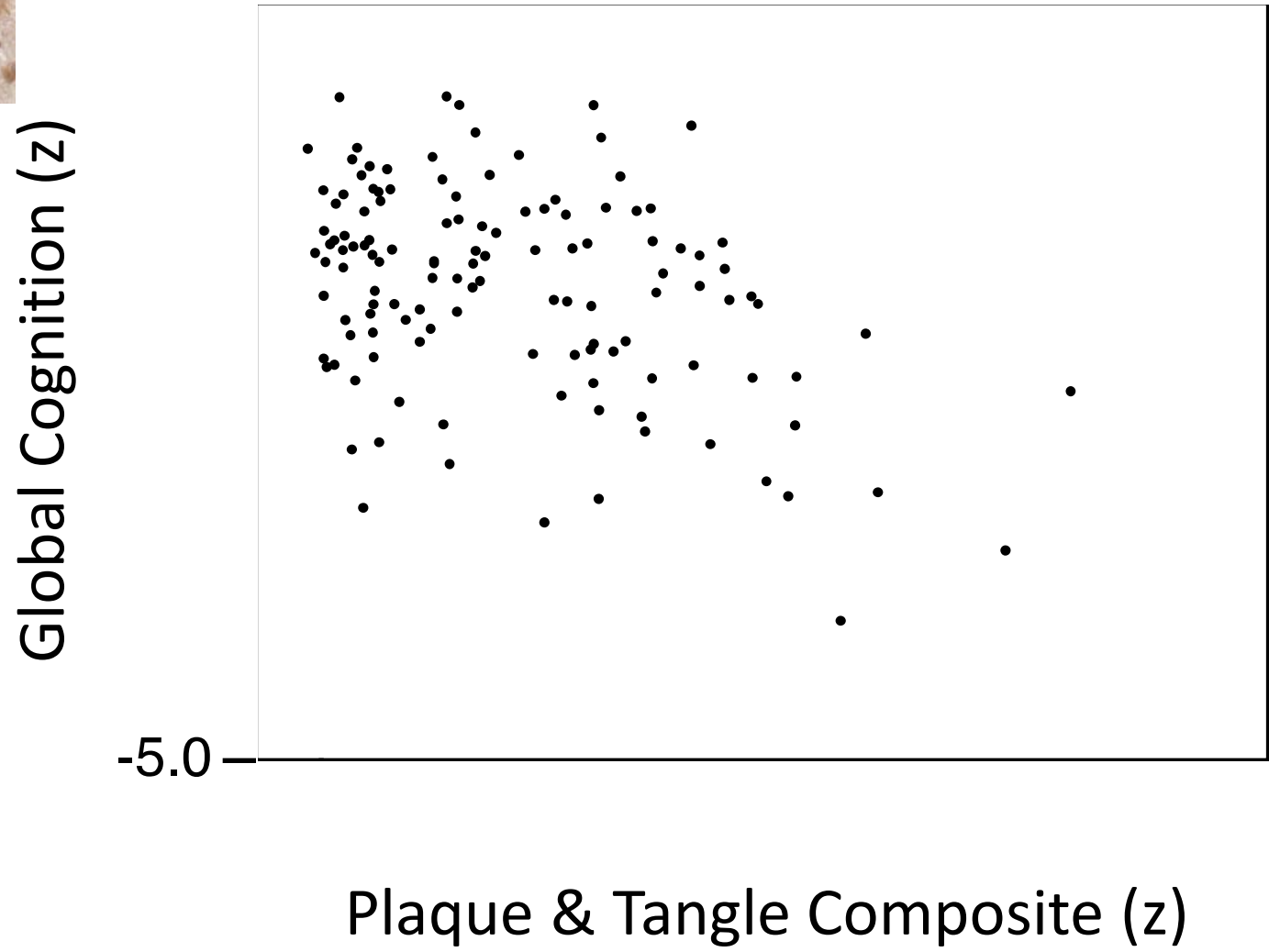
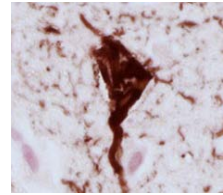
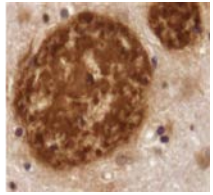


Tau PET



Association of AD Pathology with Cognition in Rush ROS and MAP*

*Adj for age, sex, educ



Some Successful Treatments for AD*

Tg2576

4-O-methylhonokiol
5-lipoxygenase (AAV)
a-lipoic acid (dietary)
Ab oral vaccine (salmonella)
Abeta-Hsp70 active immunization
Activated Protein C
Adipose mesenchymal stem cells
Aged garlic extract
AM580 (RARa)
Aminohydantoin (BACE1)
Aminoimidazoles (BACE1i)
Amniotic stem cells (TGF-b)
Anesthesia (isoflurane, propofol, others)
Antalamin (CRF1)
Anti-Ab antibody (AAV)
APP antisense oligonucleotide
APP b-secretase cleavage site antibody
AS2715348 (g-Secretase modulator)
AZ-4217 (BACE-I)
Bacaillein (flavanoid/GABA)
BAY73-6691 (PDE9A-I)
BC05 (Ab42(43) C-term antibody)
BDE-209
BDNF (SVV)
BMS-433796 (g-secretase inhibitor)
C5aR antagonist
Caffeoylquinic acid
Calorie restriction
Captopril (ACE-I)
Cerebrolysin
CHF5022 (g-secretase inhib)
CHF5074 (NSAID/g-secretase-I)
Ciproxifan (H3R antag)
COX2 inhibitor
Dates from Oman
Deferoxamine
Dihydromyricetin (flavanoid/GABA)

Dihydropyridine antihypertensives
Dihydromyricetin (flavanoid/GABA)
DP-155 (indometacin lecithin derivative)
Dihydropyridine antihypertensives
DP-155 (indometacin lecithin derivative)
Early cognitive stimulation
EGCG (green tea) + fish oil
Erythropoietin
Exercise, voluntary
Figs from Oman
Flurbiprofen
Folate (homocystein normalization)
Gastrodin
Ginkgo biloba
Ginsenoside (Ginseng)
Grapeseed polyphenols
GRL-8234 (b-secretase inhib)
GSI-953 (Begacestat, g-secretase)
Huprine X
IAC (bis(1-hydroxy-2,2,6,6-tetramethyl-4-piperidinyl) decantionat
IGF2/1 (AAV)
JNJ-40418677 (g-secr modulator)
Magnolia extract
Melatonin
Memapsin-2 (b-secrease immunization)
Minocycline
MRK-560 (g-secretase inhib)
NDP-a-MSH (Melanocortin)
Neprilysin
Neuritin (AAV)
Nicotinamide riboside (PPARg)
NNC-26-9100 (somatostatin)
oAb immunization
Obovatol
Paeonia suffruticosa

PF-04447943 (PDE9A-I)
Paeonia suffruticosa
PF-04447943 (PDE9A-I)
PF-3084014 (g-secretase)
Phenylbutyrate (HDAC-I)
Phytic acid
PN401 (uridine)
Pomegranate
Propranolol
Quadrivalent foldable Ab(1-15)(AAV)
R-flurbiprofen
Rosiglitazone
Sildenafil
SK-PC-B70M
SPI-1865 (g-secretase -I)
TAK-070 (BACE1)
TO901317 (LXR agonist)
Triflusal
Turmeric extract (optimized)
Umbilical cord blood cells
Valsartan
Vitamin D3
Walnuts
X11beta
Yokukansan
Zinc (p.o.)

Tau^{P301L} Tg

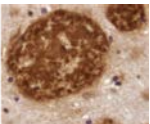
17-AAG
Deferoxamine
Grape seed polyphenolic extract
Immunization (active)
Lithium
Methylene blue

pS396/404 Tau vaccine
Sodium selenate
T-817MA (neuroprotectant)
Tau immunization
Uridine prodrug

3xTg (APP/PS1/Tau^{P301L})

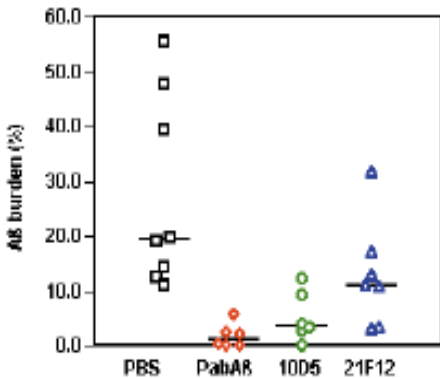
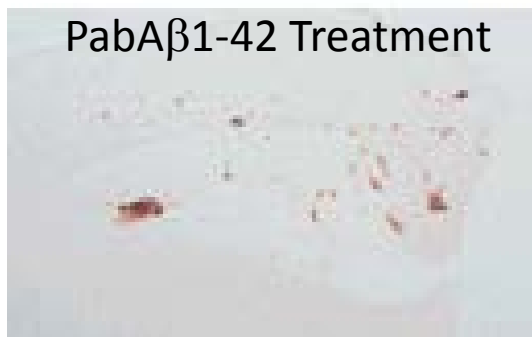
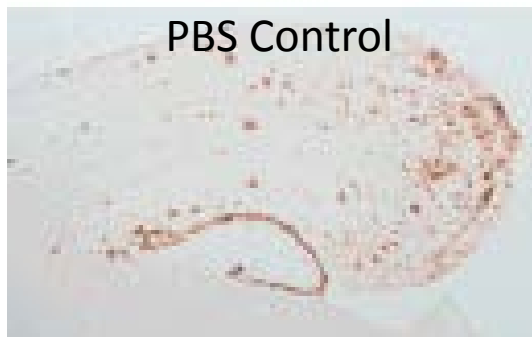
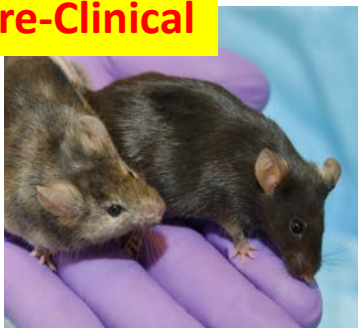
2-Deoxy-D-glucose
Allopregnalone
Apomorphine
Chinese celery extract L-NBP)
Dantrolene
Dihydrotestosterone (DHT)
Dimebon
H2S
Huperzine A (Achel)
Ibuprofen
APP b-secretase site antibody
Luprolide
Memantine
Mitoquinone (Redox)
NDP-a-MSH
Neuropep-1
phyto-b-SERM
Pioglitazone
R-flurbiprofen (NSAID)
S14G-HN Humanin
SC-560 (COX-1 inhibitor)
Spirolides
Thalidomide (TNFa)
Voluntary running
Zileuton

*** in mice, 2005-2014**



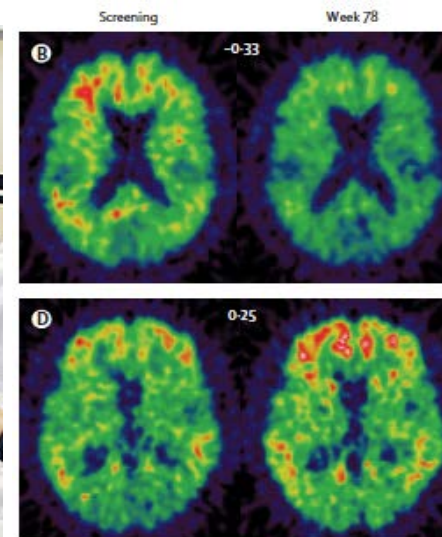
An Example of Anti-Amyloid Immunotherapy for AD

Pre-Clinical



Adapted from Bard et al, Nature Medicine, 2000

Phase 2



Phase 3

August 6, 2012 As of 7:48 PM New York 85° | 72°

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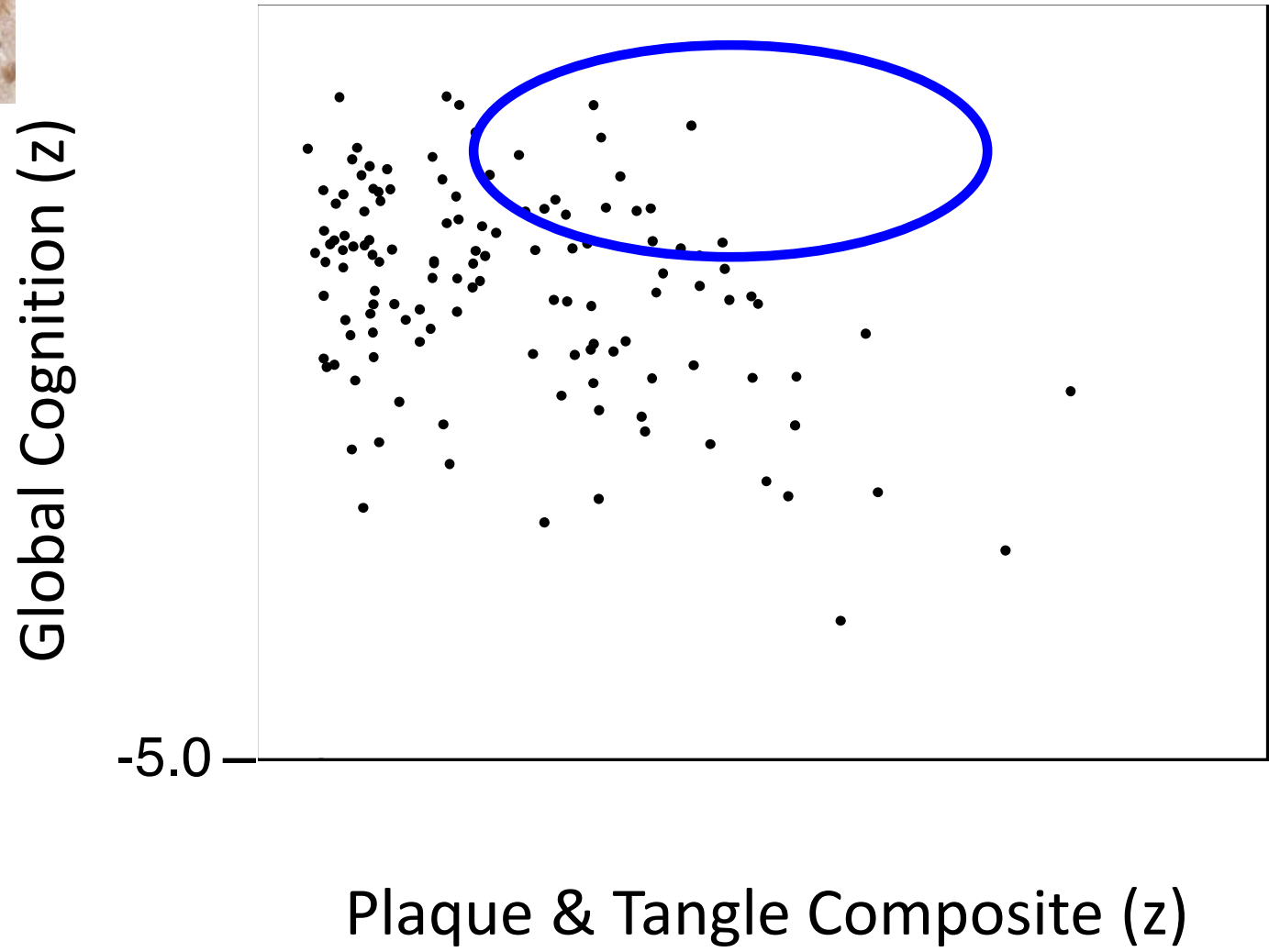
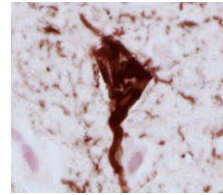
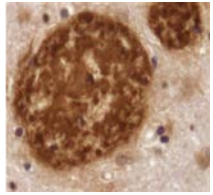
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Alzheimer's Drug From Pfizer, J&J Fails in Late-Stage Trial

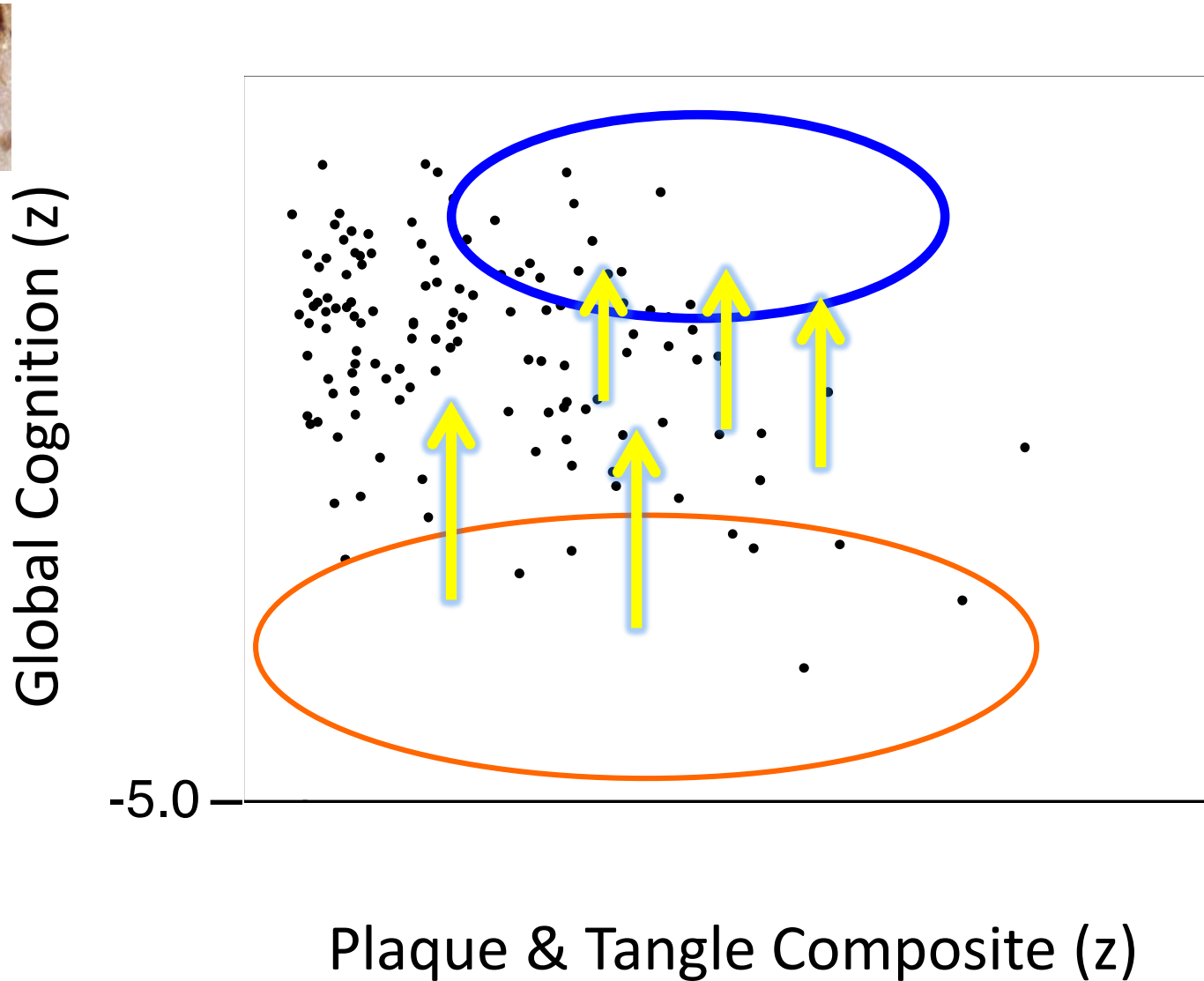
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We are all looking for the effortless magic pill for dementia but functional abilities in aging and dementia are complex and not just related to cognition but also physical conditioning and its complex relationship to brain functioning, psychosocial support and psychiatric status. So the program this afternoon is a little scientific update on each of these areas.