Hormones, Neurotransmitters & Nutraceuticals for Affective Disorders and Cognitive Enhancement

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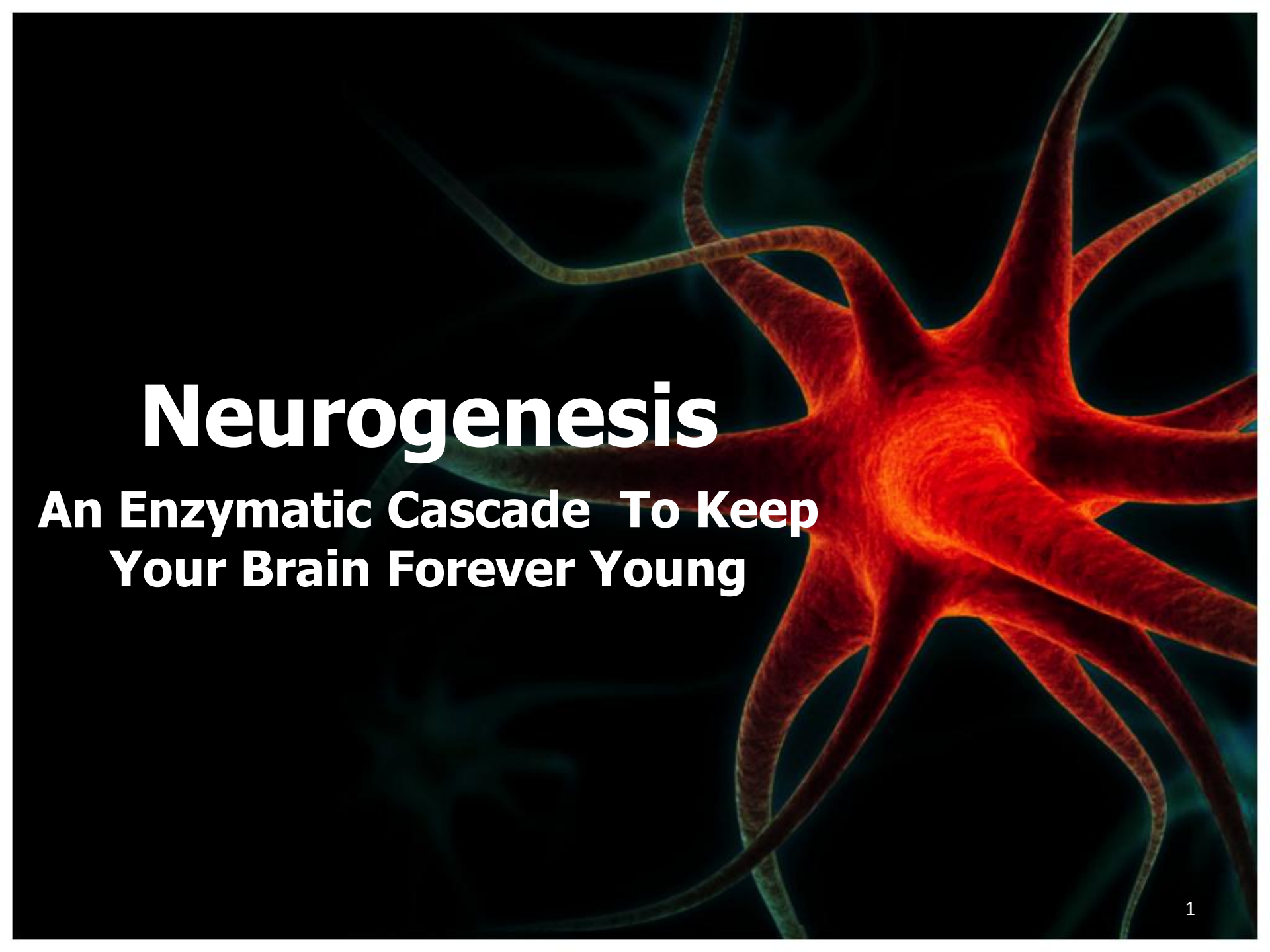


Neurogenesis

An Enzymatic Cascade To Keep Your Brain Forever Young

2 Core Principles

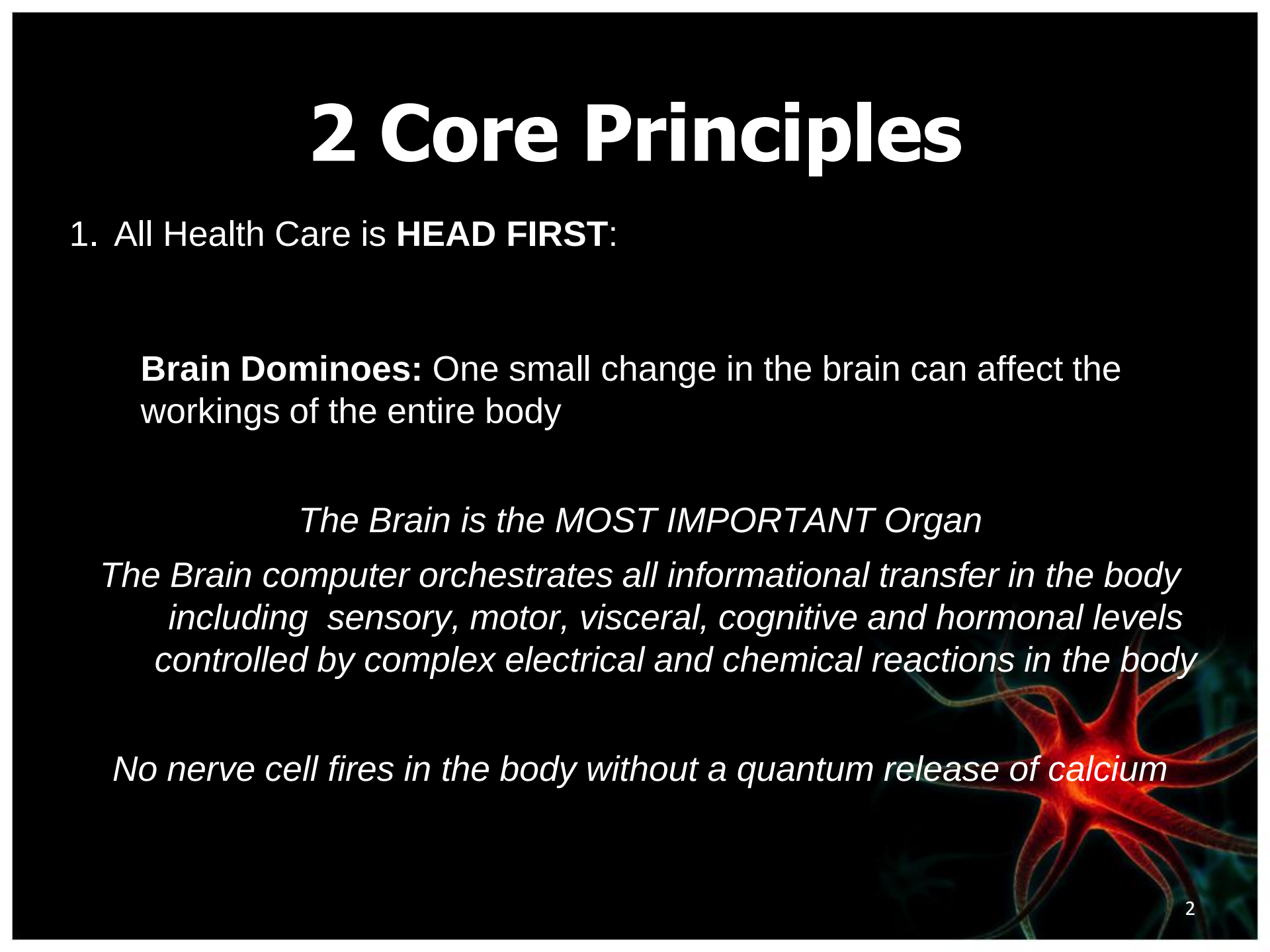
1. All Health Care is **HEAD FIRST**:

Brain Dominoes: One small change in the brain can affect the workings of the entire body

The Brain is the MOST IMPORTANT Organ

The Brain computer orchestrates all informational transfer in the body including sensory, motor, visceral, cognitive and hormonal levels controlled by complex electrical and chemical reactions in the body

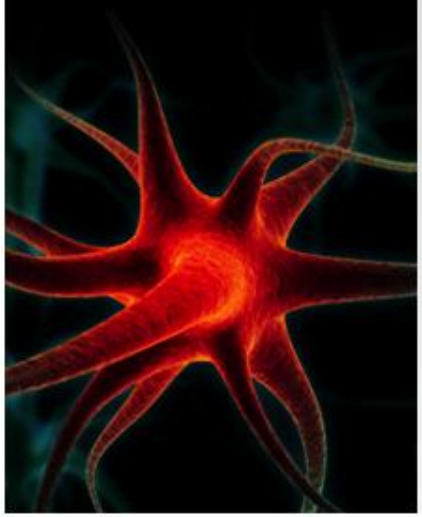
No nerve cell fires in the body without a quantum release of calcium



MCI

- MCI is generally defined as a “Mild or moderate cognitive impairment that is a ***heterogeneous*** disorder”
- It affects ***different people*** *in* ***different ways***
- *Some* cases of MCI ***turn into Alzheimer’s dementia, some remain mildly impaired*** for life, and ***others are reversed***
- With the discovery of ***neurogenesis*** – regeneration of brain cells – we can now aim to ***recover full intellectual capacities as we age***
- New vision of the future:

  Growing older could mean growing smarter, by increasing intellectual faculties



MCI and Poor Attention Span Can Kill

- In 2004, 112,012 Americans died due to attention-related accidental injuries
- That is more than 28 times the number of American deaths in Iraq!
- Loss of attention after age 30 is part of MCI
- Approximately ***50% of all adults*** partially ***fail attention tests***
- These attention and memory problems lead to deficits in IQs
- Since most of us think over a period of only ***100 msec***, a ***20% loss of our processing speed is enormous***

National Safety Council: http://www.nsc.org/lrs/statinfo/odds.htm

Early MCI

- Dementia takes 15 to 20 years to develop and begins with MCI
- Pre-MCI, asymptomatic milder form of cognitive impairment but may take another 15 to 20 years of development prior to the discovery of the first MCI symptoms
- MCI begins in the 30s-40s
- By 80-85, 50% of America is demented
- Dementia may be an accelerated form of brain aging

Modrego P.J. “The Prediction of Conversion to Dementia in Mild Cognitive Impairment by Means of Magnetic Resonance Spectroscopy and other Neuroradiological Techniques.” *Directions in Psychiatry,* Vol. 27,22; Nov 07.

High and Low Voltage Dementia

- ***Fetus to 5*** is high voltage Dementia
- ***After Age 30:*** DEMENTIA BEGINS!
- ***Age 70 and on*** is low voltage dementia→ no cell growth
- Cell growth is ***inversely*** related to Dementia
- Inability to retain memory
  - Memory was a wave and particle

General Trend of Cognitive and Physical Decline

- Loss of brain processing speed and voltage
- Loss of visual, verbal, and working memory
- Loss of complex attention
- Loss of cognition, abstract thinking ability, inductive reasoning, spatial orientation
- “Pause” of each gland and organ system
  - Anatomy begins to fail

Identifying aMCI in Primary Care

- Amnestic mild cognitive impairment (aMCI) is characterized by episodic memory impairment in the absence of clinical dementia
- aMCI represnts the transitional stage between normal aging and Alzheimer's Disease (AD)
- Patients have fewer symptoms and function better than those with mild AD; therefore, they have more ability that can be preserved with appropriate therapy
- It is not known how well non-expert primary-care physicians (PCPs) can differentiate individuals with no cognitive impairment (NCI), aMCI, and mild AD, in their own clinical settings
- A study was designed to establish the feasibility of making an aMCI designation and identifying some likely sources of error

Doody RS, et al. Identifying Amnestic Mild Cognitive Impairment in Primary Care: A Feasibility Study. *Clin Drug Investig* 2011; 31 (7): 483-491.

aMCI Feasibility Study

- 14 experts assessed subjects with memory complaints, in terms of:
  1. laboratory results
  2. MRI findings
  3. scores on the MMSE
  4. adapted Clinical Dementia Rating Scale
  5. Alzheimer's Disease Assessment Scale – cognitive subscale Delayed Word Recall
- Experts trained non-expert PCPs, using the same clinical information and utilizing the same assessment instruments
- The chance-corrected inter-rater (expert versus non-expert), based on binary outcome (aMCI/non-aMCI), was estimated
- 119 evaluable subjects were recruited (50 aMCI, 27 mild AD, and 42 NCI)

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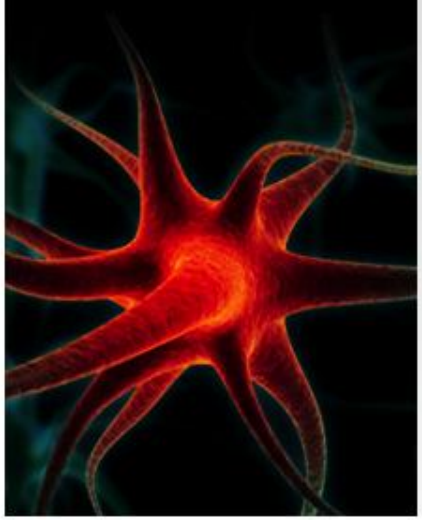

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aMCI Feasibility Study Findings

Table II. Analysis of inter-rater agreement – evaluable subjects (n = 119; binary outcome)[a]

Variable	Expert		Overall
	aMCI (n = 50)	not aMCI[b] (n = 69)	
Non-expert (n)			
aMCI	31	14	45
not aMCI[b]	19	55	74
κ			0.4229
Agreement (%)			72.3
Sensitivity (%)			62.0
Specificity (%)			79.7

a The MCI, AD and NCI classifications were based on the expert designations.

b AD and NCI subjects (pooled data).

AD = Alzheimer's disease; **aMCI** = amnestic mild cognitive impairment; **NCI** = no cognitive impairment.

Table III. Analysis of inter-rater agreement – evaluable subjects (n = 119; three-category outcome)[a]

Variable	Expert			Overall
	NCI (n = 42)	aMCI (n = 50)	AD (n = 27)	
Non-expert (n)				
NCI	37	15	4	56
aMCI	5	31	9	45
AD	0	4	14	18
Specific agreement (%)	75.5	65.3	62.2	
Sensitivity (%)	88.1	62.0	51.9	
Specificity (%)	75.3	79.7	95.6	
Weighted κ[b]				0.5698
Overall agreement (%)				68.9

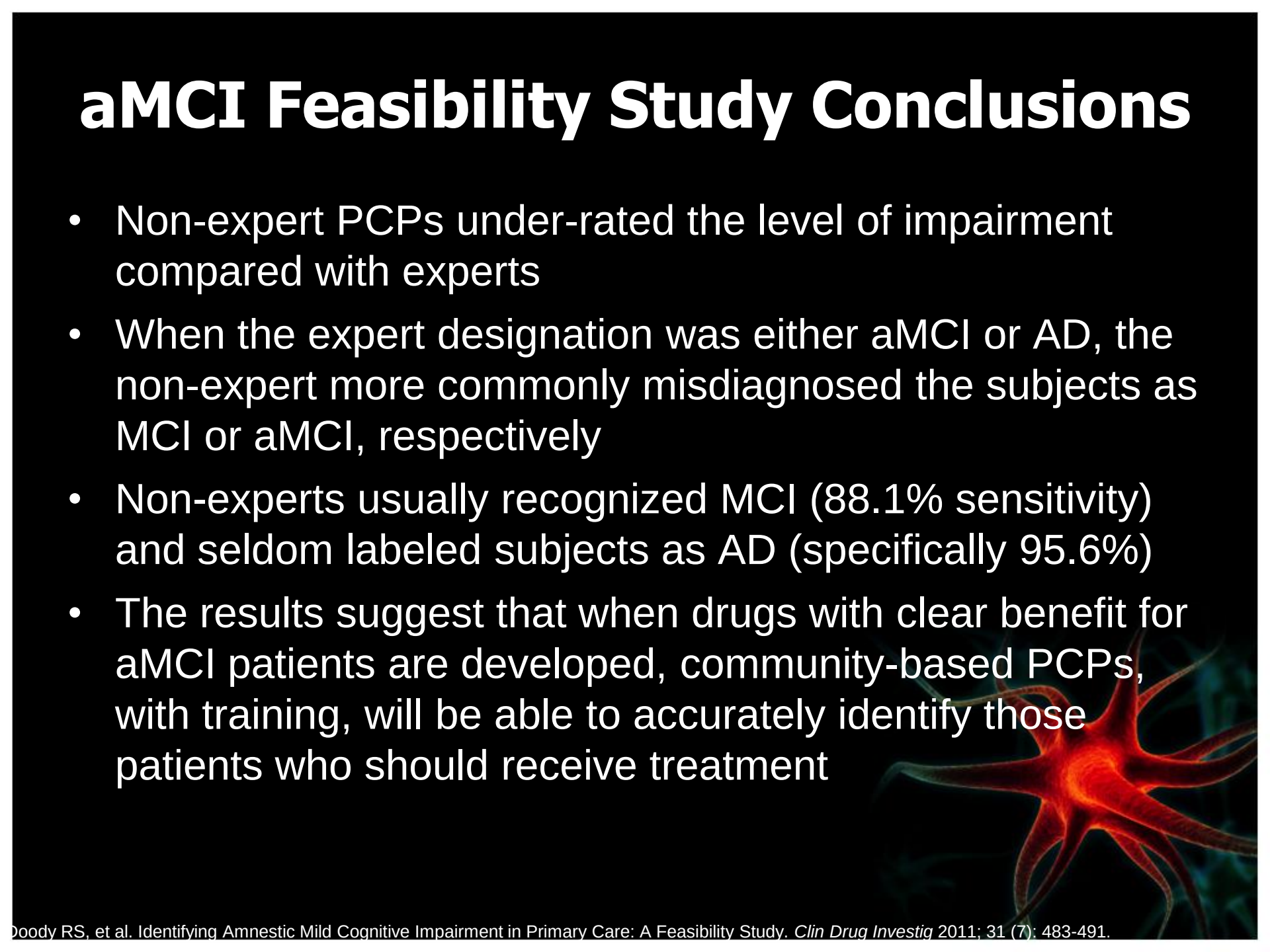
a The MCI, AD and NCI classifications were based on the expert designations.

b Calculated using Cicchetti-Allison weights.[16]

AD = Alzheimer's disease; **aMCI** = amnestic mild cognitive impairment; **NCI** = no cognitive impairment.

aMCI Feasibility Study Conclusions

- Non-expert PCPs under-rated the level of impairment compared with experts
- When the expert designation was either aMCI or AD, the non-expert more commonly misdiagnosed the subjects as MCI or aMCI, respectively
- Non-experts usually recognized MCI (88.1% sensitivity) and seldom labeled subjects as AD (specifically 95.6%)
- The results suggest that when drugs with clear benefit for aMCI patients are developed, community-based PCPs, with training, will be able to accurately identify those patients who should receive treatment



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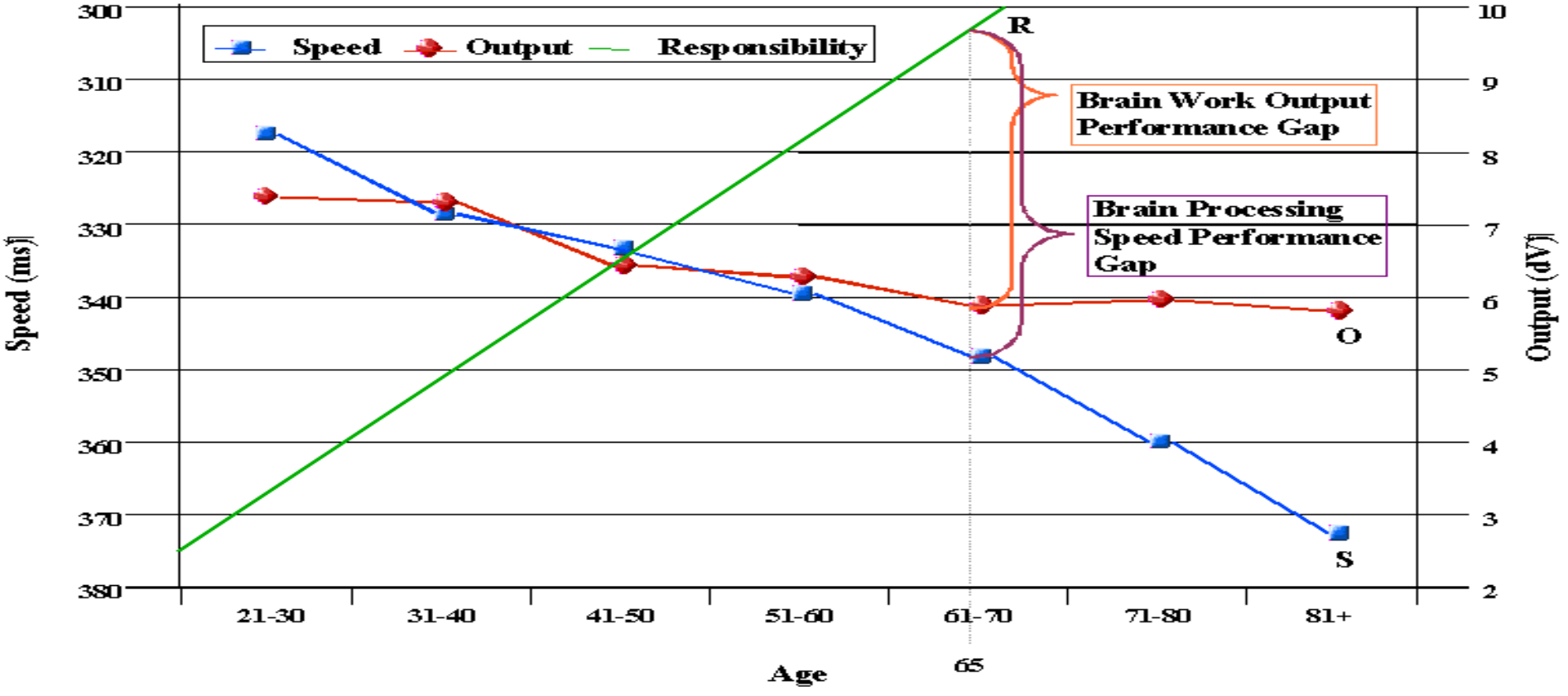
Solve Problem to Close Performance Gap

- Brain, Mind, and Physical Performance Gaps begin in the early 40s
  - Increases to dangerous levels from age 50 to 70
- This mental and physical gap can be reversed by addressing brain electrochemistry (work output and processing speed)

Braverman ER, Blum K. "P300 (Latency) Event-Related Potential: An Accurate Predictor of Memory Impairment" *Clinical Electroencephalograpy*. 2003. 34(3); 124-139.

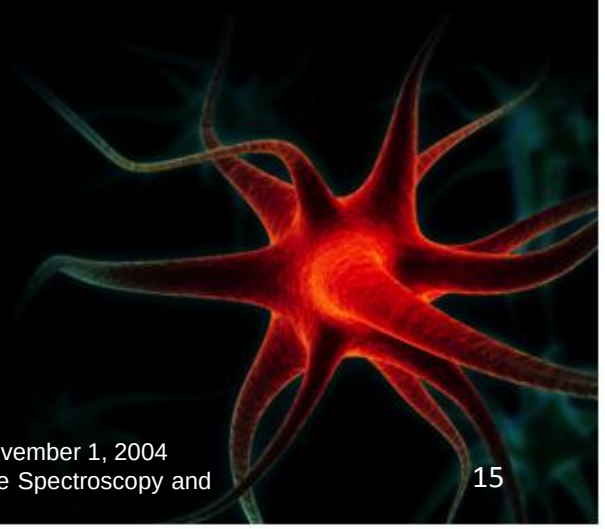


Conventional Method of Diagnosing Cognitive Impairment

- Petersen et al. advocates the combination of a skillful clinical interview, plus a judicious use of neuropsychological tests
- So far, there are no standardized tests for the evaluation of MCI

Brain Print DSM-IV Axes – Old/Traditional Method:

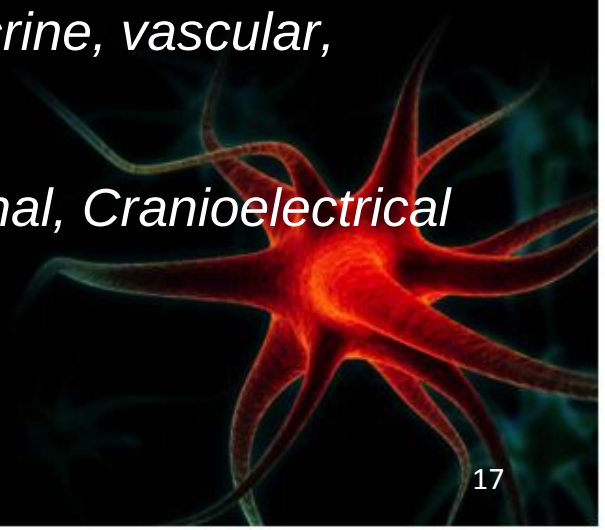
1. ***Axis I:*** **Clinical Disorders -** *bipolar, schizophrenia, etc.*
2. ***Axis II:*** **Personality Disorders -** *histrionic, dependent, schizoid, avoidant*
3. ***Axis III:*** **General Medical Conditions**
4. ***Axis IV:*** **Psychosocial and Environmental Problems**
5. ***Axis V:*** **Global assessment of functioning scale**



Sadock BJ, Sadock VA. **Kaplan and Sadock's Comprehensive Textbook of Psychiatry (2 Volume Set) 8th edition**; November 1, 2004
Modrego P.J. "The Prediction of Conversion to Dementia in Mild Cognitive Impairment by Means of Magnetic Resonance Spectroscopy and Other Neuroradiological Techniques." *Directions in Psychiatry* Vol 27, Lesson 22 November 2007.

A Novel Approach to Detecting Mental and Physical Decline

- ***Axis 0:*** **Anatomical -** *MRI, PET, CT, US.*
- ***Axis I:*** **Electrophysiological -** *speed, voltage, rhythm, synchrony* ***(BEAM)*** *qEEG, P300, AEP, VEP*
- ***Axis II:*** **Memory function (WMS III) & Attention function (TOVA and CNSVS)**
- ***Axis III:*** **Personality** and **psychiatric diagnoses, IQs (MILLON, MBTI, MMPI, psychiatric indices)**
- ***Axis IV:*** **Interfacing medical problems -** *endocrine, vascular, metabolic, immunologic, genetic etc.*
- ***Axis V*****: Treatment -** *Neurotransmitter & Hormonal, Cranioelectrical and Nutritional Therapies*



Progression to Cognitive Failure

Brain

Toxic exposure/TBI/Hypoxia

↓

Hyperlipidemia

↓

Hypertension

↓

Cerebrovascular Disease

↓

Cerebral Ischemia/Infarct or demyelination

↓

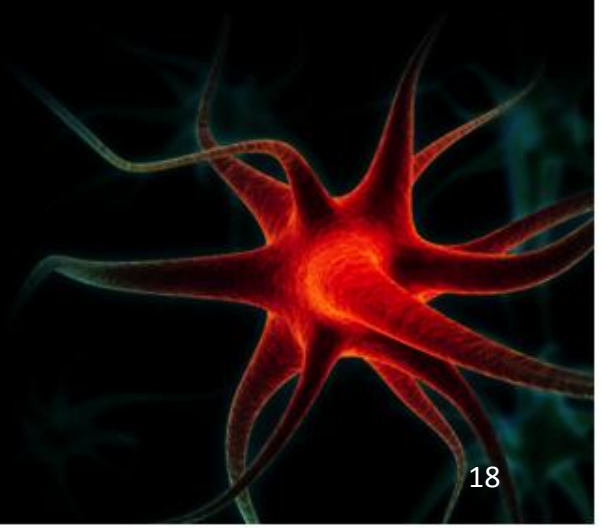
Neurodegenerative Cascade

↓

Mild Cognitive Impairment

↓

Dementia/Death



Progression to Dementia

Brain

↓

↓

Depression/Tremors/Attention(Dopamine)

↓

Depression/Insomnia (Serotonin/Melatonin)

↓

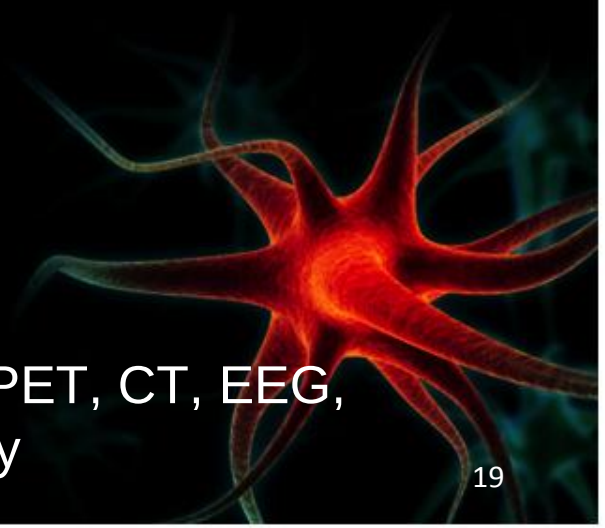
Depression/MCI(ACH)

↓

Anxiety/Tremors (GABA)

↓

Dementia (ALL)



* Evaluate through full brain and body MRI, PET, CT, EEG, ultrasound and blood chemistry

Progression to Brain Death

The Aging Brain

↓

Cellular DNA Damage to Telomeres

↓

Lamin A

↓

Nucleus Integrity

↓

DNA Replication

↓

Telomerase

↓

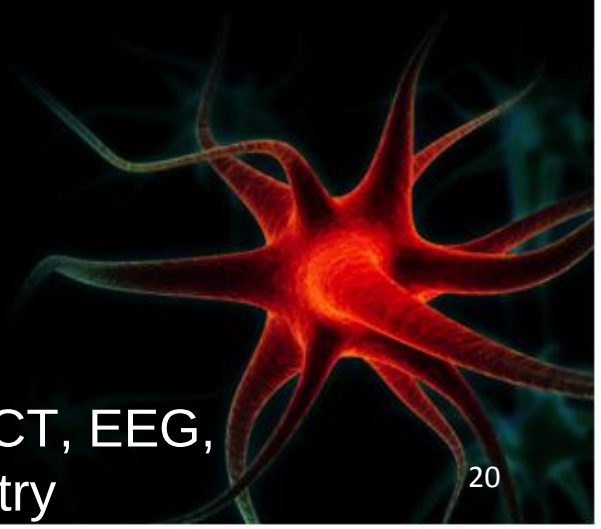
Metabolic Damage

↓

Atrophy

↓

Brain Death



* Evaluate through brain MRI, PET, CT, EEG, ultrasound, and blood chemistry

The Brain: Electrophysiological Diagnostic Evaluation

- **P300:** voltage (strength) and latency (delay in the wave echo)
- **Evoked potentials** (using visual and auditory provocations): numbers
  - **Grade of abnormality:** Grade 1 through 7
- **Spectral analysis:** including changes in frequency of the alpha wave
  - ***Synchrony*** **(On/Off Switch) Mind - Body Relaxation**
- **EEG Electroencaphalography**

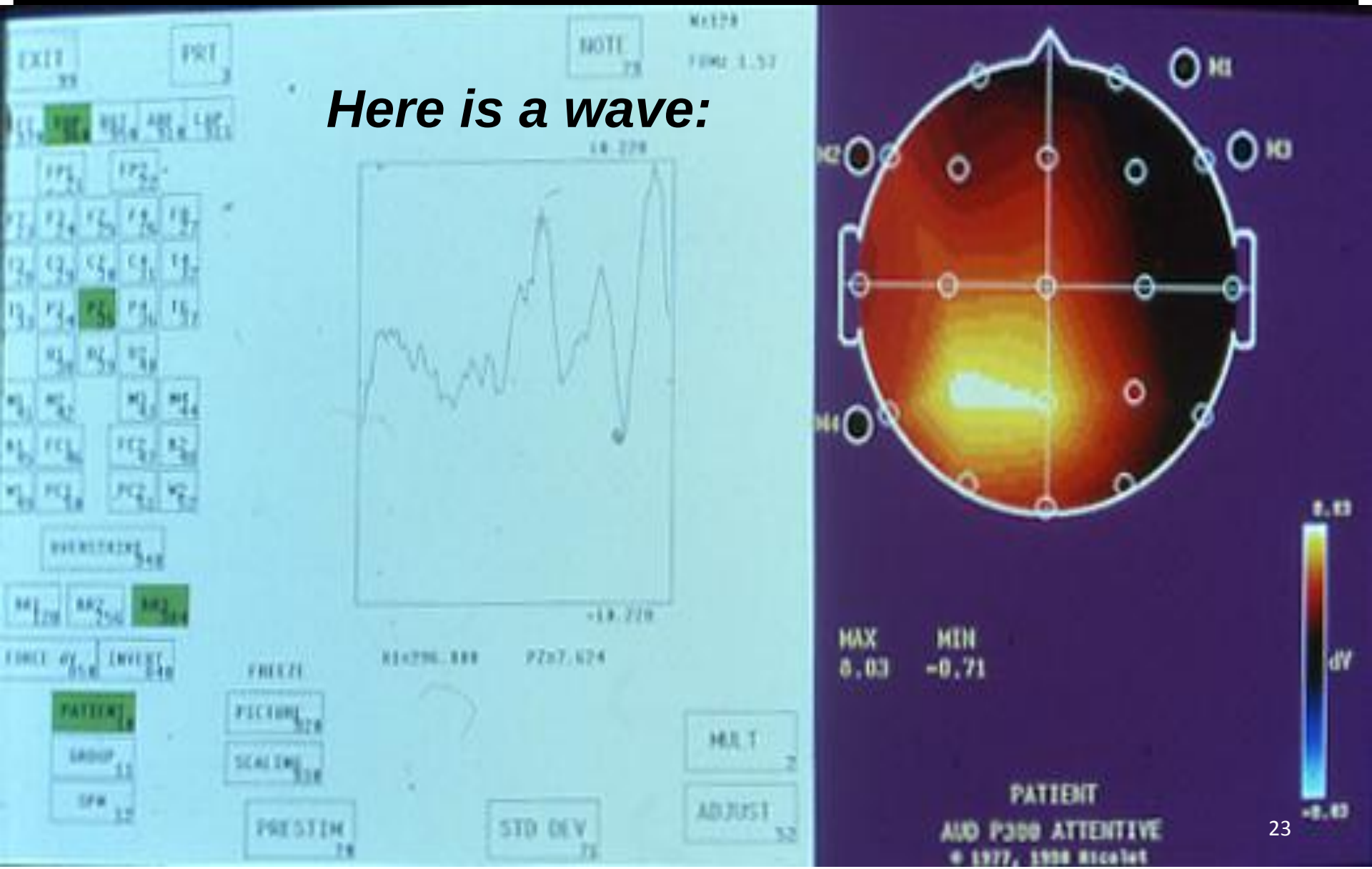
Brain Print Levels of Cognitive Impairment

Electrophysiology - Key to Brain Health:

1. **Speed:** Quickness
2. **Voltage:** Muscle Power
3. **Rhythm:** Endurance
4. **Synchrony:** Coordination
5. **Distraction Detector:** P300 catches the inattention, the blocking effect of loss of focus

Delayed P300 latency correlates with abnormal Test of Variables of Attention (TOVA) in adults and predicts early cognitive decline

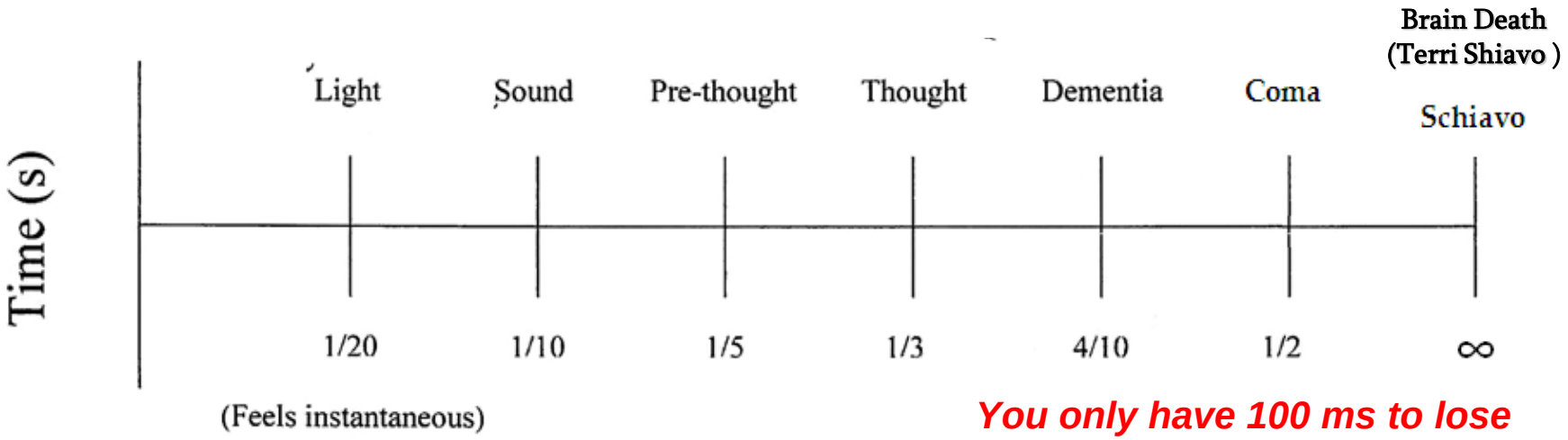
Brain Speed and Voltage Measured by P300 Wave



Age (years)	P300 speed (msec)	P300 Voltage (mV)	Neurocognitive Changes in Relation to Health
2	380	15	Infantile Amnesia, Delayed Brain speed but High Voltage Energy
12	360	12	Surge of Hormones, Confusion
20	320	10	Maturing and Peak Vibrancy
30	330	9	Cognitive Decline
40	340	8	More Memory and Attention loss and Cognitive Decline
50	350	7	Ambush of Internal Silent Disease
60	360	6	Severe Chronic Illness, Massive Brain and Body Performance Gap
70	370	5	Critical Dementia, No Cell Growth
80	380	4	Increased Loss

The Human Computer Reaction

Brain speed and reaction time deteriorates with aging



You only have 100 ms to lose in the course of your life

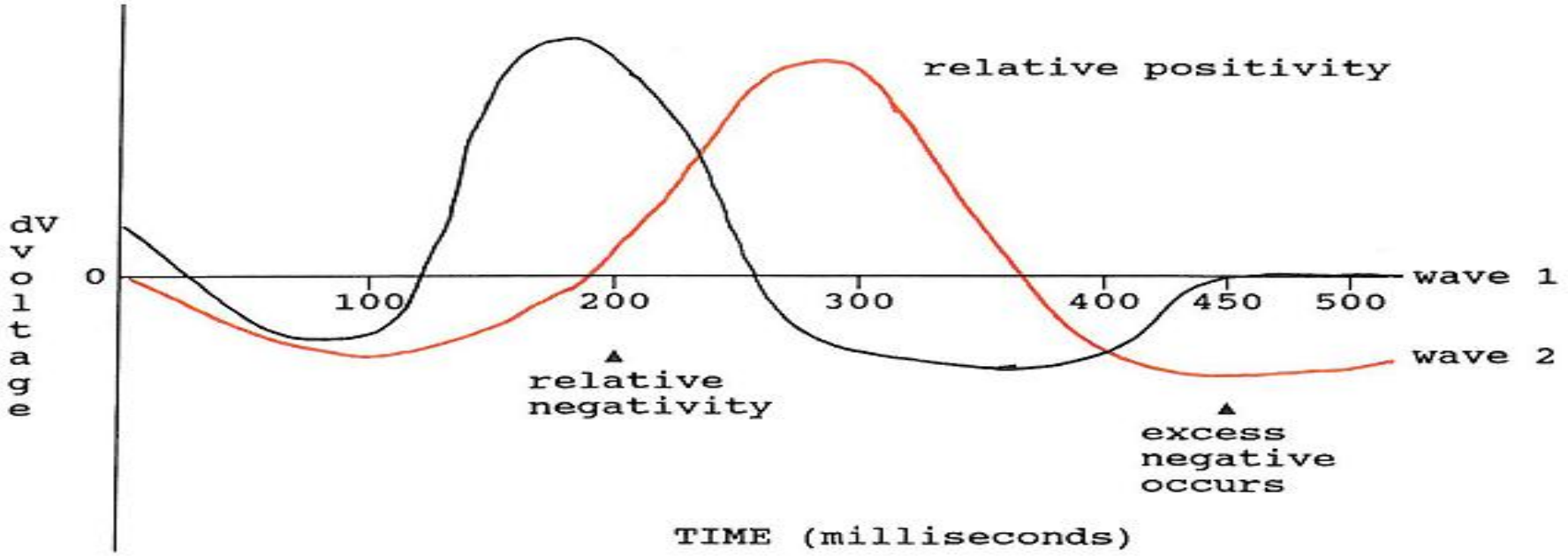
Most people lose 7ms per decade

Human Reaction Speed

Normal vs. Abnormal Evoked Potentials

- Two waves: One is control and other is that of a patient (delayed)
  - Beginning: Normal
  - At 200 ms: relative negativity
  - At 300 ms; relative positivity
  - At 450 ms: excess negative
- Wave 2 abnormalities result from delay of Evoked Potential
- **The question is really: How your brain is out of rhythm in relation to normally functioning brains?**

It's not the Vertical Shift in the Sine Curve, it's the Horizontal Shift!



Memory Loss Early On: Predictor of Future MCI

Pre-Cognitive Decline:

1. Verbal memory – 64%
2. Visual memory – 97%
3. Visual motor speed – 79%
4. Reaction time – 39%
5. <.05

Post-Cognitive Decline:

1. Verbal memory – 42%*
2. Visual memory – 85%
3. Visual motor speed – 70%
4. Reaction time – 18%*

- ***A patient asks, "Why am I in the neurosurgery department?"***
  - The visualization of head trauma, head injury and its impact on several brain problems is best identified through software developed by the neurosurgical department at the University of Pittsburgh, Dr. Joe Maroon, Vice Chairman of the Department of Neurological Surgery.

Covassin T., Stearne D., and Elbin R. "Concussion history and post-concussion neurocognitive performance and symptoms in collegiate athletes." *J Athl Train*. 2008 Apr-Jun;43(2):119-24

CNS Vital Signs

Appreciation for a tool that ***objectively measures cognitive state:***

- reaction time relay
- reduced psychomotor speed

Each of us has a different brain print:

- Unfortunately, we do not know our brain print now
- So, when we are injured, it is hard to pick up subtle abnormalities
- However, each of us has a scattergram of performance cues

Depicts a Scattergram of Performance

CNS Vital Signs Clinical Report	Test Date: September 17 2009 15:17:56
Subject ID:	Administrator: administrator
Language: English (United States)	Age: 40

Above average domain scores indicate a standard score in that domain of greater than 109. Average is 90-109. Low Average is 80-89. Below Average is 70-79. Very Low is less than 70. Reaction times are in milliseconds. An * denotes that "lower is better", otherwise higher scores are better.

Patient Profile:	Percentile Range			> 74	25 - 74	9 - 24	2 - 8	< 2
	Standard Score Range			> 109	90 - 109	80 - 89	70 - 79	< 70
Domain Scores	Subject Score	Standard Score	Percentile	Above	Average	Low Average	Low	Very Low
Neurocognition Index (NCI)	NA	53	1					x
Memory	82	69	2					x
Verbal Memory	47	82	12			x		
Visual Memory	35	67	1					x
Processing Speed	47	89	23			x		
Executive Functioning	-1	42	1					x
Psychomotor Speed	155	86	18			x		
Reaction Time*	687	92	30		x			
Complex Attention*	49	-21	1					x
Cognitive Flexibility	-4	40	1					x
Total Test Time (min:secs)	28:37			Total time taken to complete the tests shown.				

http://www.cnsvs.com

Brain Levels of Attention Impairment

These are the causes of accidents, such as friendly fire, etc:

Various forms of Attention that can be impaired:

- TOVA
- Omissions- Missed Stop Signs
- Commissions- Jump the gun!
- Response Time- Slow
- Response Variability- Inconsistent
- Complex Attention- Cannot pull it together

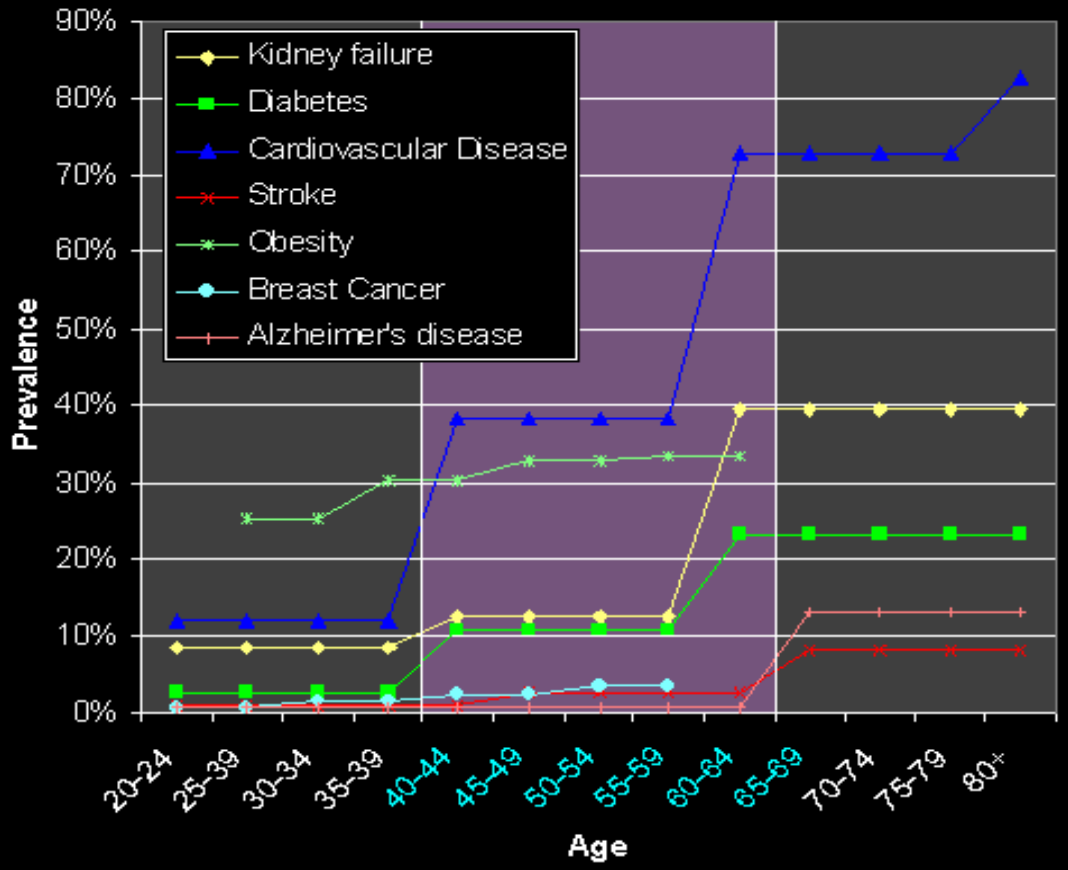
Independent cognitive effects of atrophy and diffuse subcortical and thalamico-cortical cerebrovascular disease in dementia." Swartz RH et al Stroke 2008 Mar;39(3):822-30

Millon Clinical Multiaxial Inventory -III

- Schizoid (91)
- Dependant
- Avoidant (84)
- Histrionic
- Narcissistic (75)
- Antisocial (81)
- Aggressive/Sadistic (67)
- Compulsive
- Passive-Aggressive
- Self defeating

- Schizotypal (76)
- Borderline (84)
- Paranoid (90)
- Anxiety Disorder (94)
- PTSD (105)
- Dysthymic (99)
- Alcohol Dependence (67)
- Drug Dependence (65)
- Thought Disorder (75)
- Major Depression (87)
- Delusional Disorder (95)

Increase in Age-Related Disease Parallels Cognitive Decline



Taking off of disease begins in early 40s and explodes in mid 50s

While disease is increasing, the brain is traumatized by additional injuries, for example from sports and combat

http://www.americanheart.org

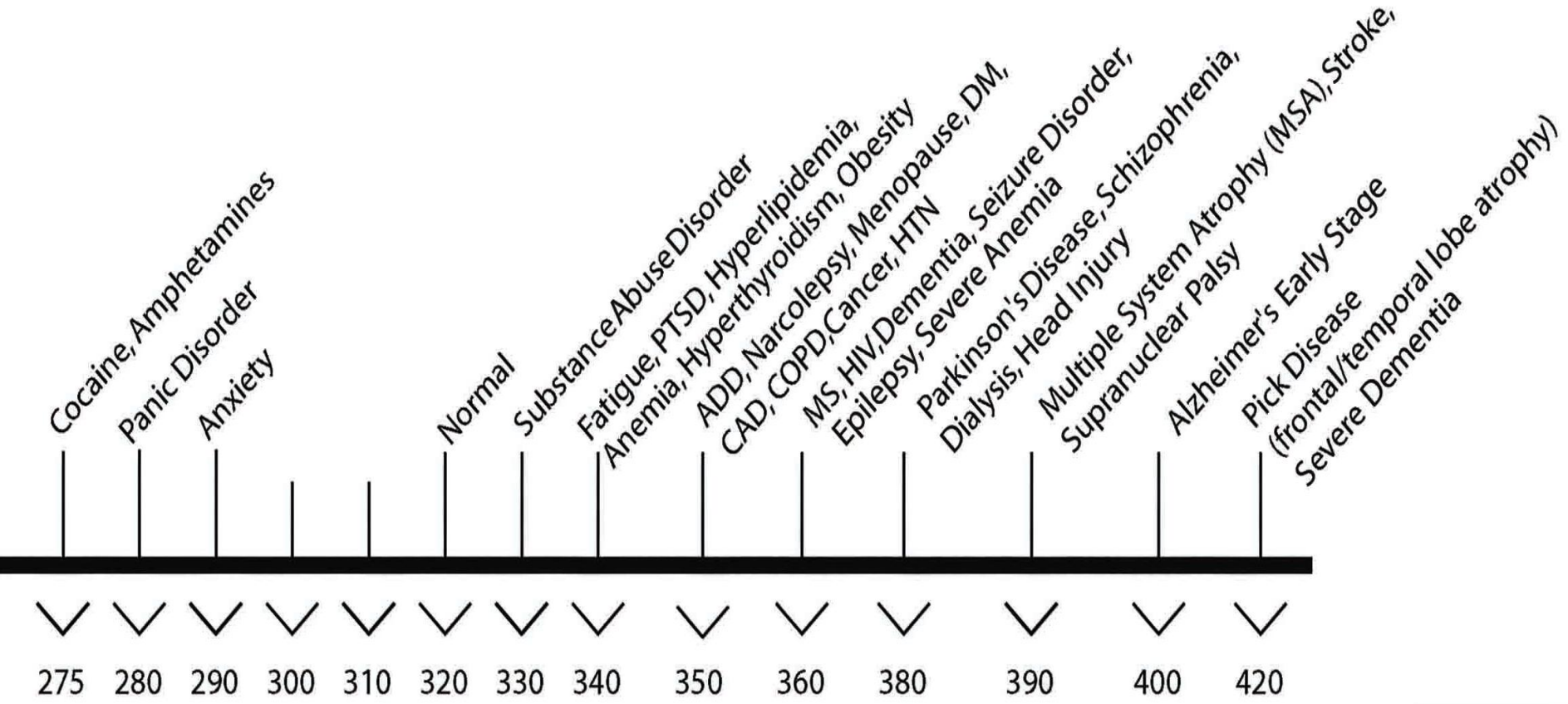
http://www.cdc.gov

http://obesity1.tempdomainname.com

ttp://www.alz.org/national/documents/report_alzfactsfigures2009.pdf

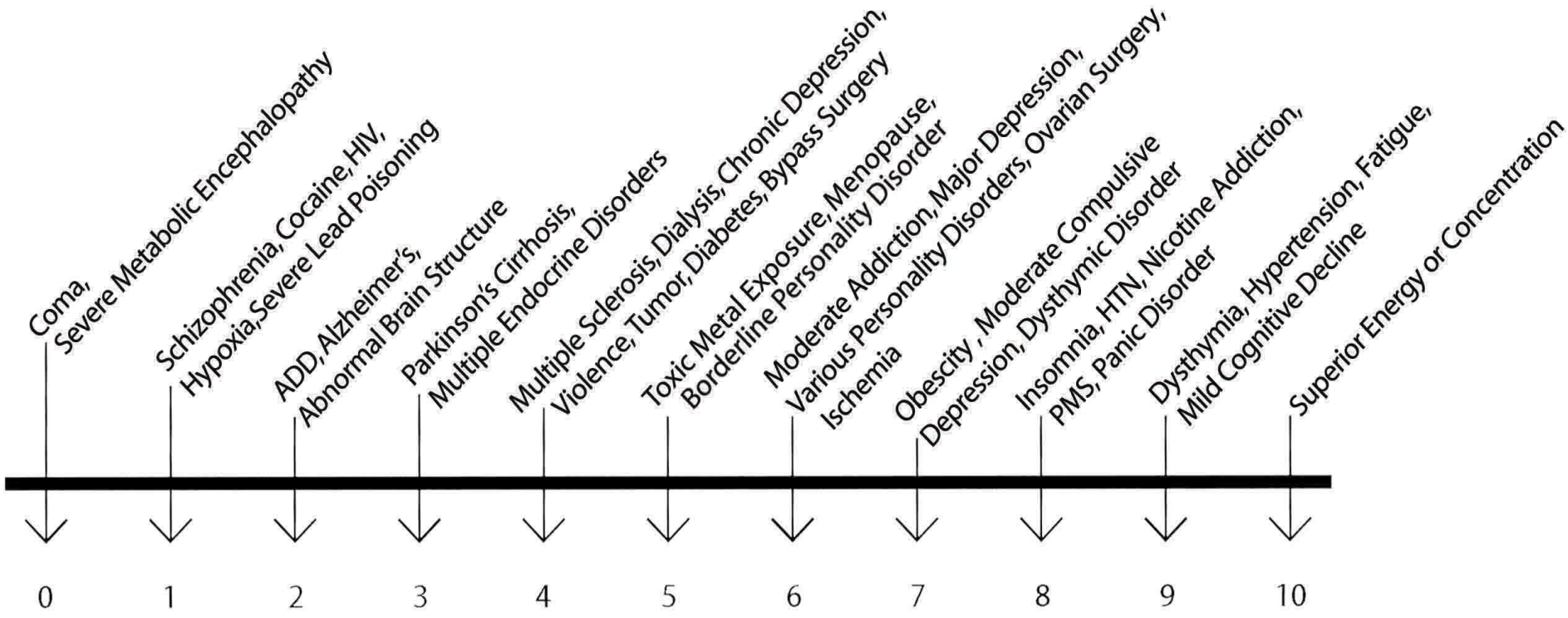
CDC. Prevalence of chronic kidney disease and associated risk factors – United States, 1999-2004. MMWR Morb Mortal Wkly Rep. 2007 Mar 2;56(8):161-5

All Medical Illnesses Affect Brain Electrophysiology: Brain Speed Damage by Aging



Impact of Breakdown on Brain Voltage

We look at the voltage of the P300 wave.
Whereas normal expectations are 10 mV (microvolts), deviances indicate abnormal brain wave function:



Hormonal Decline Predicts Performance Gap That Can Be Repaired, Otherwise Memory And Attention Deficits Will Occur

Age 30 → HGH, IGF-1,3 deficiency

Age 40 → Testosterone, Estrogen deficiency

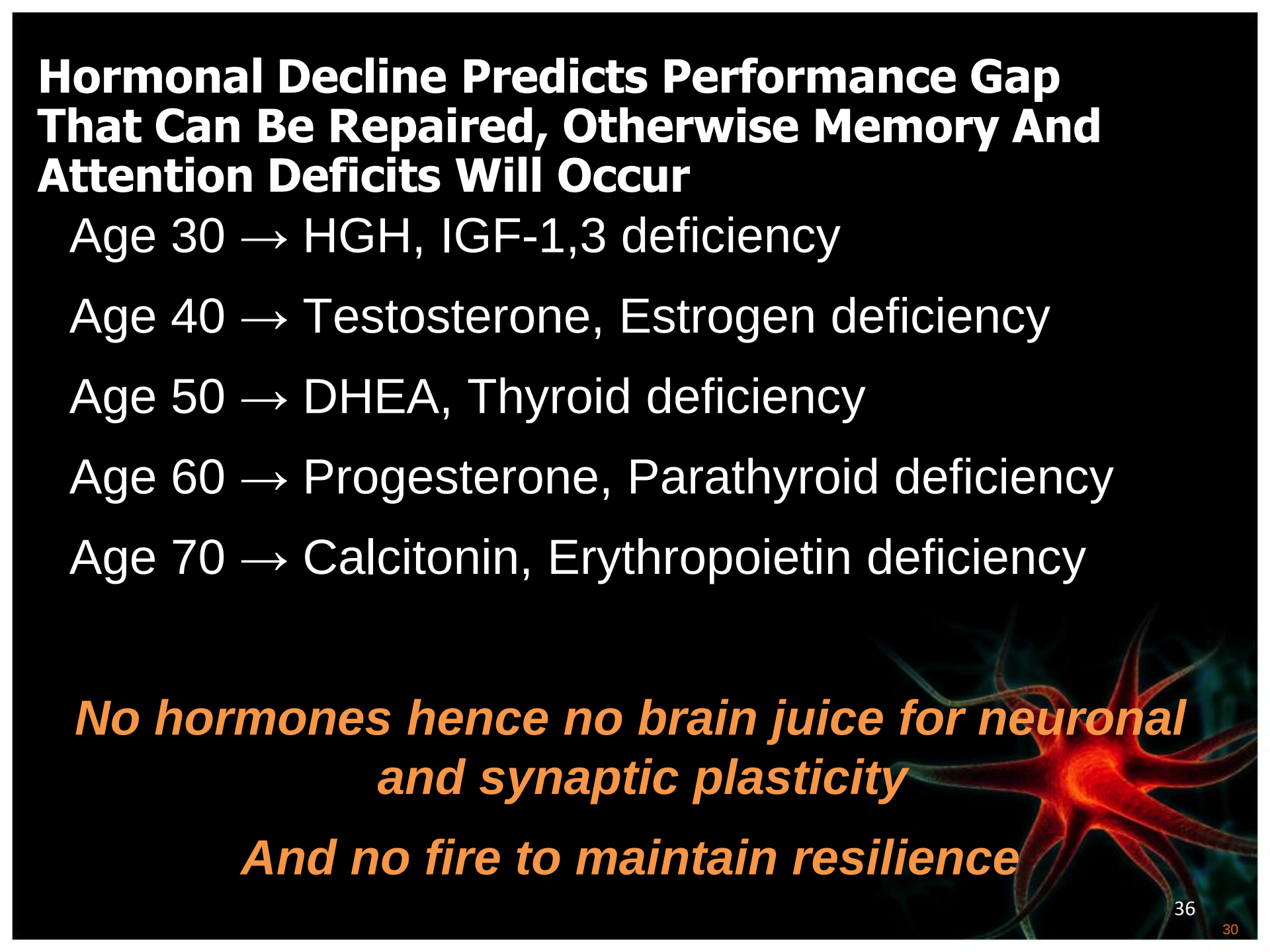
Age 50 → DHEA, Thyroid deficiency

Age 60 → Progesterone, Parathyroid deficiency

Age 70 → Calcitonin, Erythropoietin deficiency

No hormones hence no brain juice for neuronal and synaptic plasticity

And no fire to maintain resilience

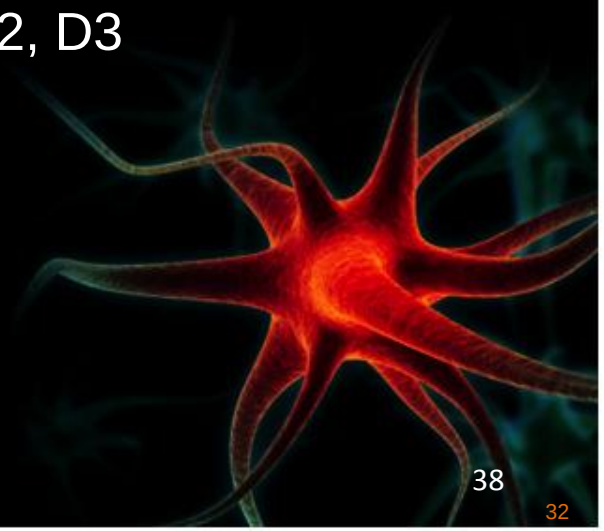


Loss of Neurotransmitters and Hormones due to Aging Leads to Widespread Breakdown

Delerium/Confusion- Dopamine ↓	Dementia- Acetylcholine ↓	Depression- Serotonin ↓	Anxiety/Panic- GABA deficiency ↓
Hypo/Hyperglycemia	Hypothyroidism	Hyperthyroid	Hyperthyroidism
Hypothyroidism	Vitamin B12 Def.	Adrenal Insuff.	Hypopituitarism
Hypopituitarism	Diabetes Mellitus	Hypopituitarism	
Vitamin B Defic.	Hypopituitarism	Diabetes Mellitus	
Hypercalcemia	↓ Leptin	Hypercalcemia	
		↑ Leptin	

Hormones Imbalances That May Contribute to Cognitive Decline:

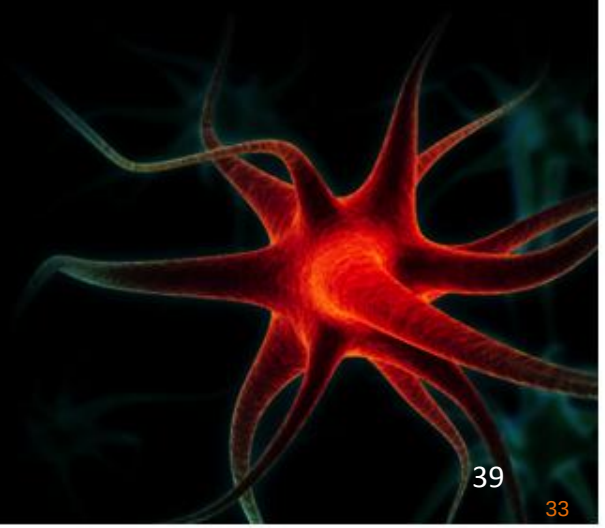
- Androstenedione
- Calcitonin
- Dehydroepiandrosterone (DHEA)
- DHEA-Sulfate (DHEA-S)
- Erythropoietin
- Estriol
- Estrone
- Human growth hormone (HGH)
- Hydroxycortisol/aldosterone
- Insulin-like growth factor (IGF)
- Incretin (at least 50% bioidentical)
- Insulin
- Melatonin
- Parathyroid Hormone
- Pregnenolone
- Progesterone
- Testosterone
- Thyroid: T3, T4
- Vitamins D2, D3
- Oxytocin
- DDAVP



Brain or the Mind

- Which came first: The ***neuronal*** or the ***psychiatric deterioration?***

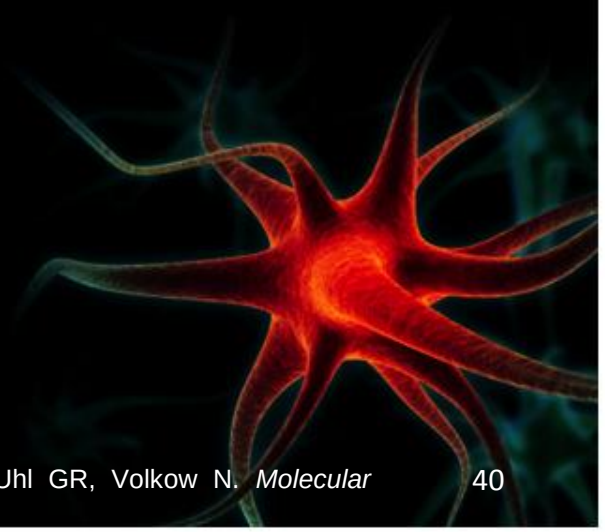
Answer: The ***gene!*** Neurological and psychiatric decline occur ***concomitantly.***



Genetic Factors & Phenotypes

- People with certain ***DRD2 gene polymorphisms*** may have psychiatric conditions such as:

1. Aggression
2. antisocial personality
3. conduct disorder
4. social alienation/schizoid personality
5. social phobia/avoidant personality
6. ADHD
7. Binging
8. stress reactions
9. abnormal visual evoked response
10. abnormal P300 amplitudes and latency



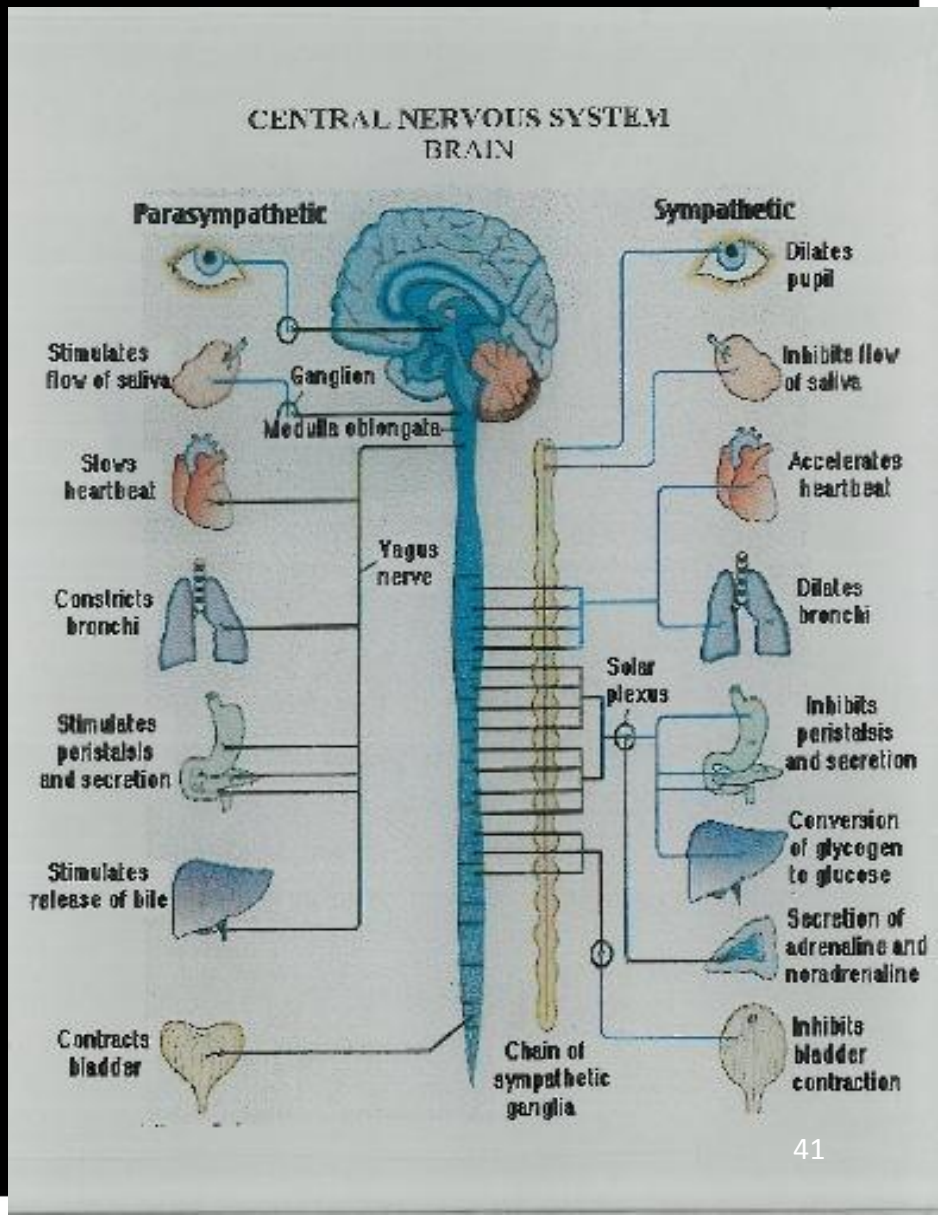
"Perspectives on Reward Circuitry, Neurobiology, Genetics and Pathology: Dopamine and Addiction." Uhl GR, Volkow N. *Molecular Psychiatry* Vol 6, Suppl 1 Feb 2001

The Key to Reversing Mental and Physical Decline: Treating the Brain

The Brain is Your Most Important Organ:
It Affects the Functioning of the Entire Body

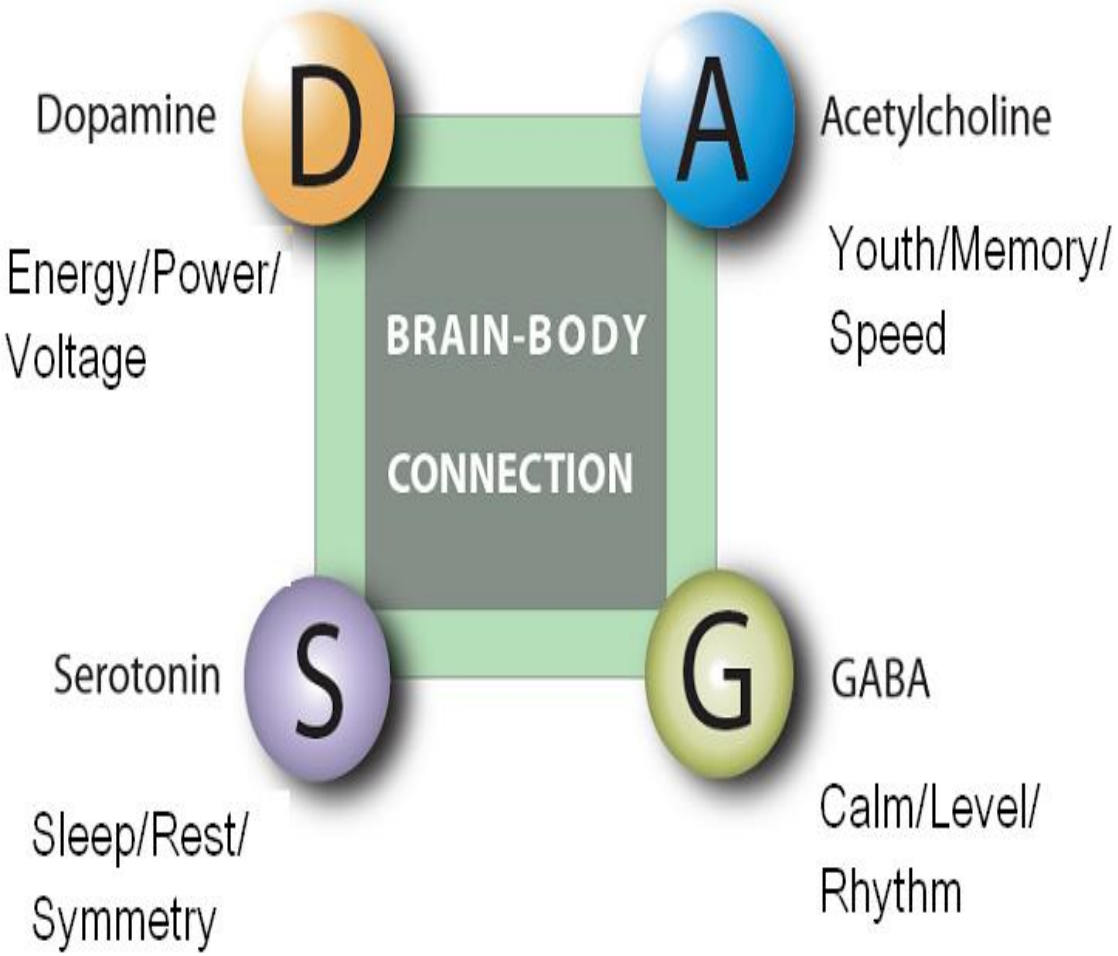
One critical system is ***NOT*** under our control: Autonomic Nervous System

- Regulated ONLY by neurotransmitters & hormones



Neurotransmitter Integration

Balancing all neurotransmitters results in quantum neurologic enhancement



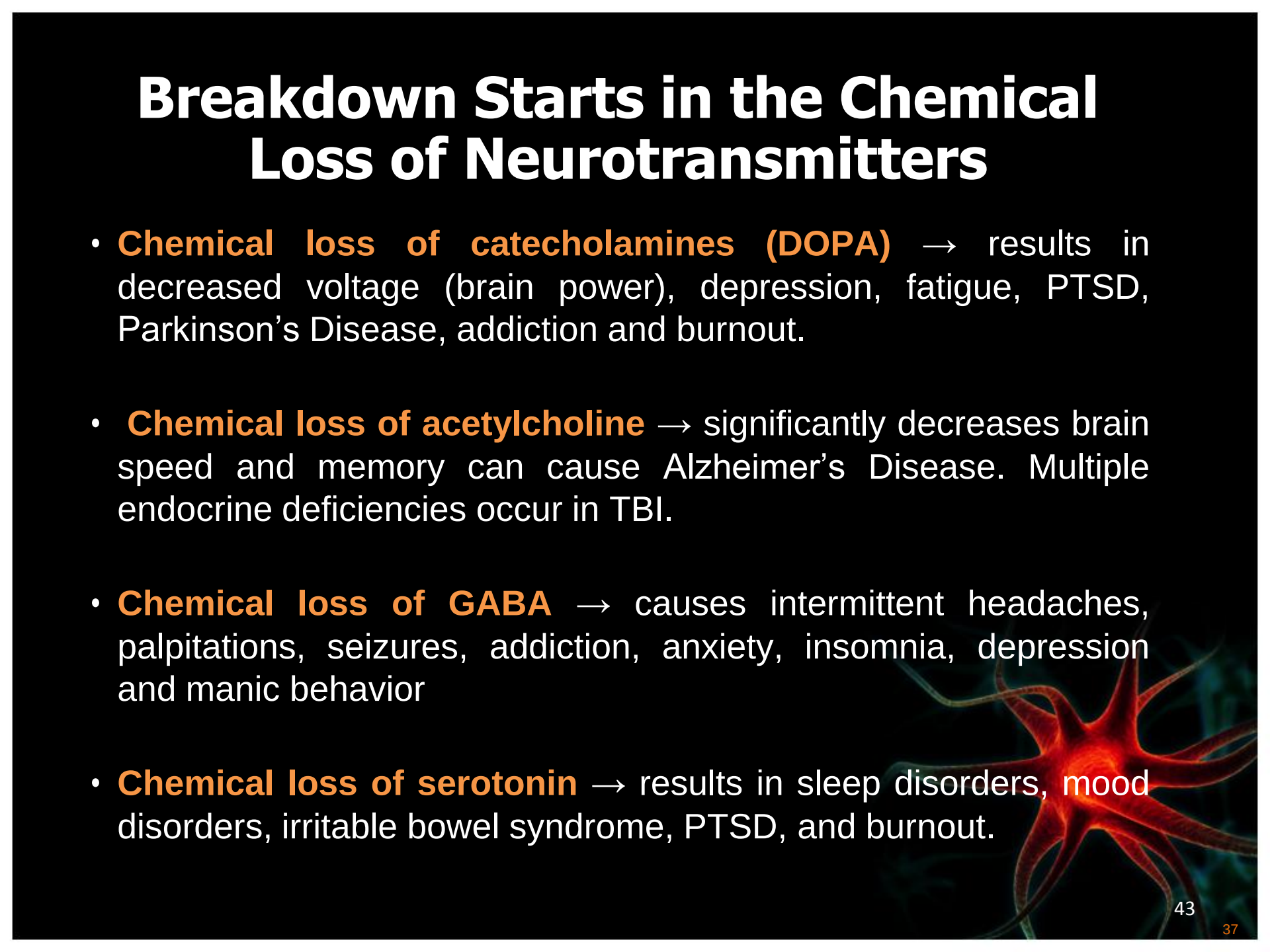
Breakdown Starts in the Chemical Loss of Neurotransmitters

- **Chemical loss of catecholamines (DOPA)** → results in decreased voltage (brain power), depression, fatigue, PTSD, Parkinson's Disease, addiction and burnout.

- **Chemical loss of acetylcholine** → significantly decreases brain speed and memory can cause Alzheimer's Disease. Multiple endocrine deficiencies occur in TBI.

- **Chemical loss of GABA** → causes intermittent headaches, palpitations, seizures, addiction, anxiety, insomnia, depression and manic behavior

- **Chemical loss of serotonin** → results in sleep disorders, mood disorders, irritable bowel syndrome, PTSD, and burnout.



Brain and Body Repair Mechanisms

System	Natural	Pharmaceutical	Hormonal	Electrical Treatments & Lifestyle Changes
Dopamine "Energy, Power & Voltage"	Caffeine Rhodiola Rosea Folic acid Tyrosine	Wellbutrin Tenuate Provigil Cymbalta	Testosterone/Estrogen DHEA Thyroid	Weight bearing exercise Teas Spices: Cumin, etc
Serotonin "Sleep, Rest & Symmetry"	Fish Oils Tryptophan Magnesium Resveratrol	SSRI's SNRI's	Progesterone Pregnenolone	CES/TENS Sleep Complex Carbs
Acetylcholine "Youth, Memory & Speed"	Fish oils Choline Lipoic Acid	Aricept Exelon Statin drugs Namenda	Estrogen Parathyroid	Aerobics Spices: Sage Eggs, etc
GABA "Calm, Constancy & Rhythm"	Inositol CoQ Theanine	Depakote Topamax	Progesterone Human Growth Hormone	CES Spices: Cinnamon

The Binary Neuro-Electrochemical System: The Order

Dopaminergic (catecholamines)
Cholinergic

> +

GABAergic
Serotonergic

> -

Endorphins – “spare tires”

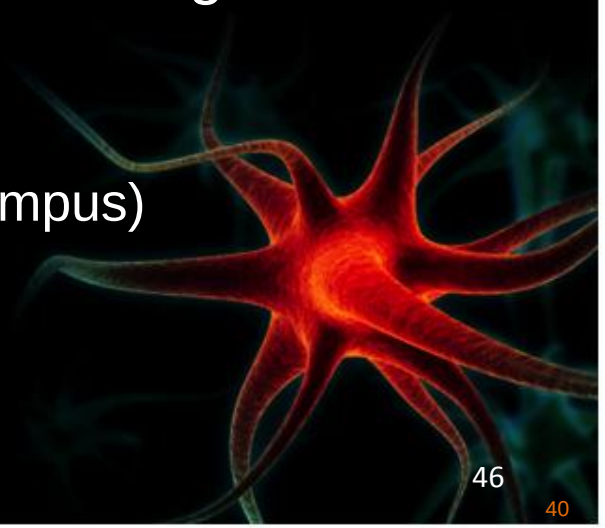
Clark Randt showed that ***adrenaline*** helps with ***memory***

E=MC²
Cognitive Energy=Brain Speed x (Voltage)²

Brain cyclic AMP and memory in mice Randt CT et al *Pharmacol Biochem Behav.* 1982 Oct; 17(4):677-80

How do Hormones Enhance Brain Speed?

- Many of the same hormones associated with increases in processing speed are also associated with neurogenesis, or growing new brain cells (Hgh, Pregnenolone)
- These hormones may make it possible to grow smarter as we grow older!
- Antidepressants are known stimulants of neurogenesis
  - Improve P300 latency in depressed patients
  - Improve Brain Atrophy (especially in hippocampus)



Parathyroid Hormone/Thyroid Hormone Therapy

- Parathyroid hormone levels increase with age and have shown a positive correlation with P300 latency
- Control of PTH levels may be an important factor in protecting against age-induced dementia
- Hyperparathyroidism and osteoporosis can lead to calcifications in brain and body
- Thyroid hormones have been shown to modulate adult hippocampal neurogenesis in studies on rats
- Hypothyroidism is associated with poor concentration, memory disturbances, depression, and decreased cognitive function, and is linked to increased P300 latency

Brain Calcification due to secondary hyperparathyroidism in a child with chronic renal failure." Blige I et al *Turk J Pediatr* 2005 Jul-Sep;47(3):287-290

Subclinical hyperparathyroidism, an age dependent phenomenon, is an antecendent of both osteoporosis (OP) and dementia." Braverman E, Arcuri V, Blum K *Alzheimer's and Dementia* Vol 3, issue 3, p S133-S134

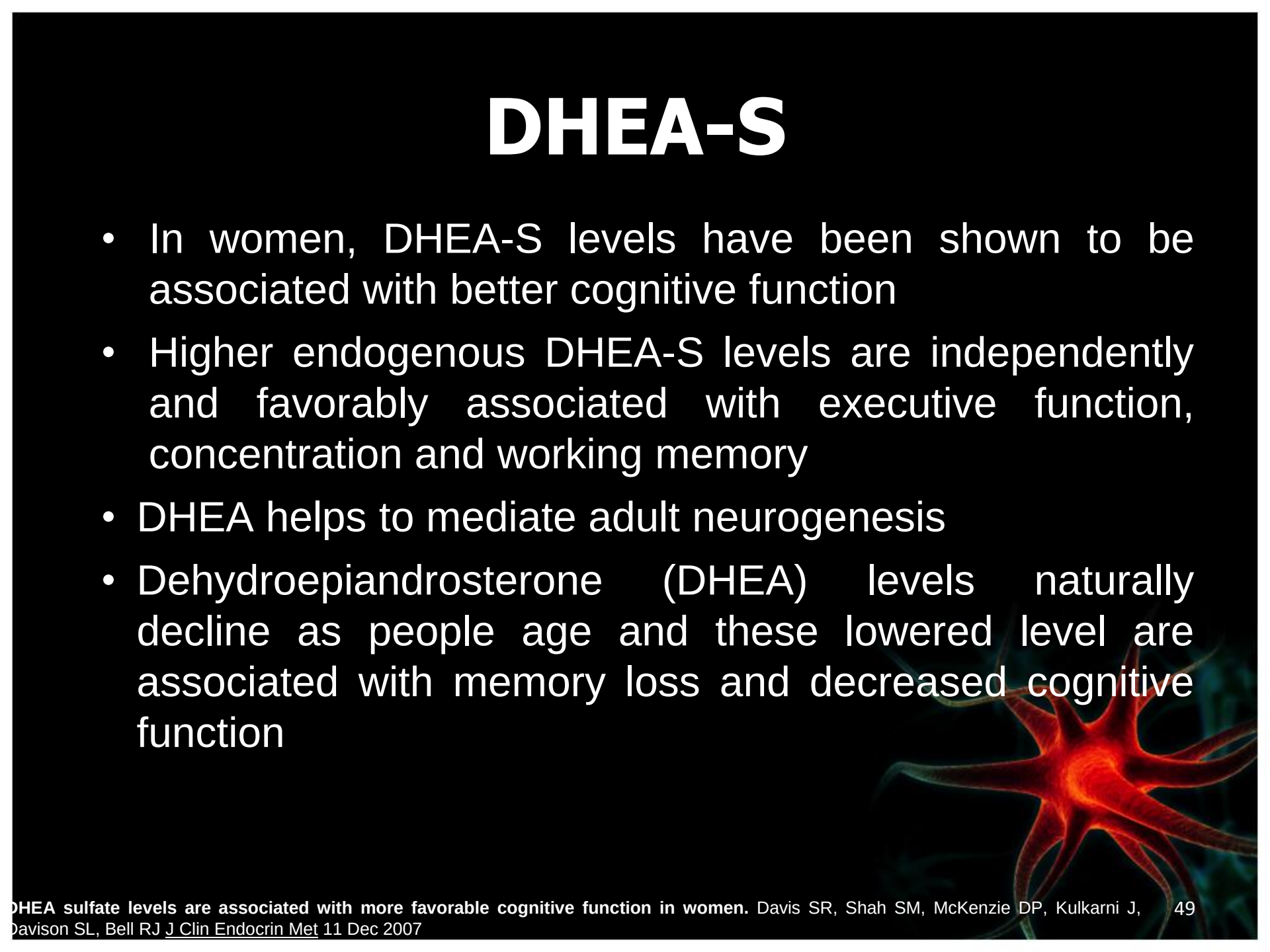
Estrogen Replacement Therapy/ Testosterone Therapy

- Estrogen replacement therapy in menopausal women has led to a significant improvement in information processing as indexed by a significant shortening of P300 latency
- Estrogen pretreatment attenuated the anticholinergic drug-induced impairments on attention tests
- Serum testosterone levels positively correlate with brain speed, and have been shown to enhance adult hippocampal neurogenesis
- Androgen therapy may thus be used to prevent Alzheimer's dementia and other forms of cognitive decline.

Androgen regulation of beta-amyloid protein and the risk of Alzheimer's disease Rosario ER, Pike CJ Brain Res Rev. 2008 Mar;57(2):444-53
"Estrogen Treatment Effects on Anticholinergic-Induced Cognitive Dysfunction in Normal Postmenopausal Women." Dumas J, Hancur-Bucci C, Naylor M, Sites C, Newhouse P *Neuropsychopharmacology* 2006 31, 2065-2078.
"Age-related cognitive decline in the menopause: effects of hormone replacement therapy on cognitive event-related potentials." Anderer P, Saletu B, Gruber D, Linzmayer L, Semlitsch HV, Saletu-Zyhlarz G, Brandstatter N, Metka M, Huber J *Maturitas* 2005 Jul 16;51(3):254-69

DHEA-S

- In women, DHEA-S levels have been shown to be associated with better cognitive function
- Higher endogenous DHEA-S levels are independently and favorably associated with executive function, concentration and working memory
- DHEA helps to mediate adult neurogenesis
- Dehydroepiandrosterone (DHEA) levels naturally decline as people age and these lowered level are associated with memory loss and decreased cognitive function



DHEA sulfate levels are associated with more favorable cognitive function in women. Davis SR, Shah SM, McKenzie DP, Kulkarni J, Davison SL, Bell RJ J Clin Endocrin Met 11 Dec 2007

Growth Hormone Therapy

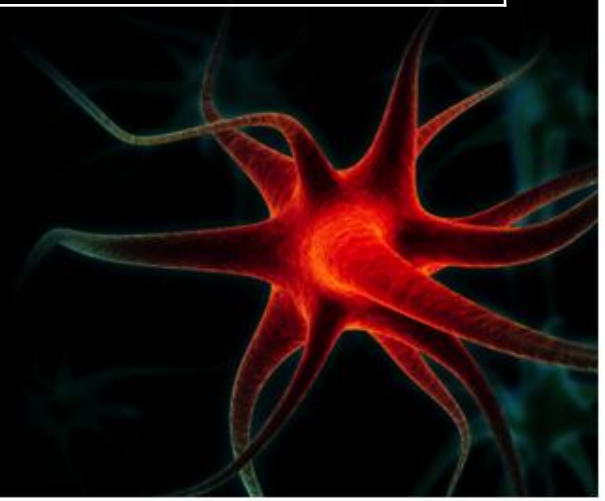
- In patients with growth hormone (GH) deficiency, GH replacement therapy decreased P300 latency after 6 months
- Low IGF-1 correlates to delayed processing speed, a loss of 10-20 msec

Braverman ER, Chen T, Prihoda T, Sonntag W, Meshkin B, Downs W, Mengucci J, Blum S, Notaro A, Arcuri V, Varshavskiy M, Blum K. "Plasma Growth Hormones, P300 Event-Related Potential and Test of Variables of Attention (T.O.V.A) Are Important Neuroendocrinological Predictors of Early Cognitive Decline in Clinical Setting: Evidence SUPPORTED BY structural Equation Modeling Parameter Estimates." *Age*. 2007 Sep;29(2-3):55-67.

Golgeli A, Tanriverdi F, Suer C, Gokce C, Ozesmi C, Bayram F, Kelestimur F. "Utility of P300 auditory event related potential latency in detecting cognitive dysfunction in growth hormone (GH) deficient patients with Sheehan's syndrome and effects of GH replacement therapy." *Eur J Endocrinol.* 2004 Feb;150(2):153-9.

Nutritional Therapies that Enhance Cognitive Function

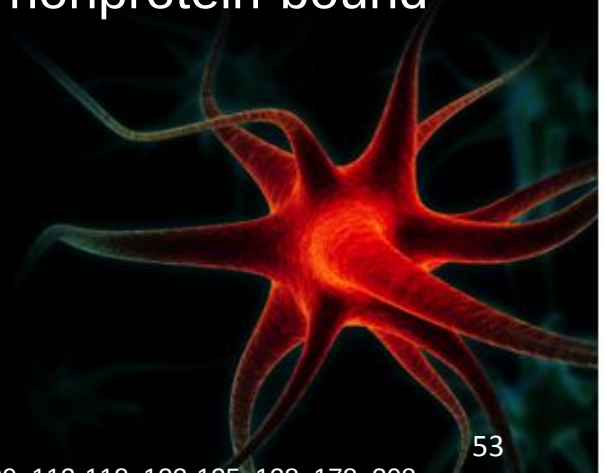
Vitamin and Mineral Antidotes
Coriander, Garlic, Calcium, Magnesium, Kelp, Gingko Biloba, Green tea, Peppermint, Cysteine, Cystine, Methionine, Taurine, Melatonin, Iodine, Selenium, Folic Acid, Vitamin E, Spirulina, Ashwagandha, Methionine, Alginates, Iron, Selenium, Zinc, Vitamins A, B1, C, Pectin, Copper



N-Acetyl L-cysteine and Radiation

A Model for Nutrient Therapeutics:

- ❖ Inhibit irreversible photobinding
- ❖ Improve radiation tolerance
- ❖ Inhibit potassium channel activation by gamma radiation
- ❖ Decreases C-JUN MRNA (also H2O2 induced)
- ❖ Increases clonogenic survival
- ❖ Decreases accumulation of P53
- ❖ Increases total nonprotein-bound thiols



Braverman, Eric "The Healing Nutrients Within ". Basic Health Publications Inc. 2003. P12, 50, 77, 104, 107-109, 112-118, 123-125, 128, 178, 308.

N-Acetyl L-cysteine and Radiation

A Model for Nutrient Therapeutics:

- UVA and UVB rays (reduce oxygen intermediate species)
- Lymphocytes
- Inhibit NF Kappa B
- Ethyl ester form
- Topical application

- Decreases EGF (epidermal) tyrosine phosphorylation
- Decreases PGE2 synthesis
- Increases epidermal phospholipases
- Increases GSH content
- Decreases DNA breaks (parents cells, deletions, dicentrics)

Braverman, Eric "The Healing Nutrients Within ". Basic Health Publications Inc. 2003. P12, 50, 77, 104, 107-109, 112-118, 123-125, 128, 178, 308.

Neurogenesis: The New Treatment For Aging Brains

REPLENISH damaged brain cells with fresh ones:

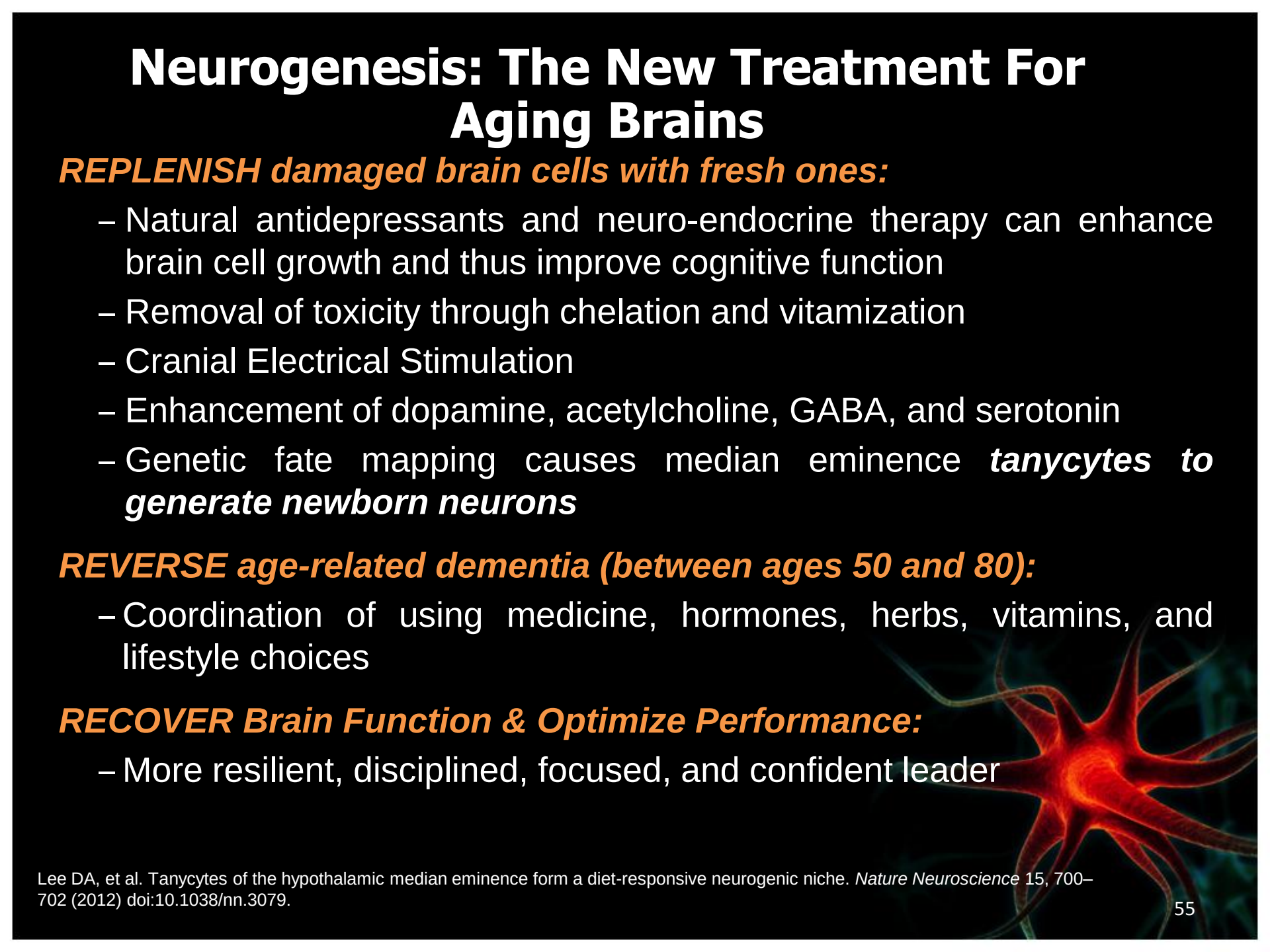
- Natural antidepressants and neuro-endocrine therapy can enhance brain cell growth and thus improve cognitive function
- Removal of toxicity through chelation and vitamization
- Cranial Electrical Stimulation
- Enhancement of dopamine, acetylcholine, GABA, and serotonin
- Genetic fate mapping causes median eminence ***tanycytes to generate newborn neurons***

REVERSE age-related dementia (between ages 50 and 80):

- Coordination of using medicine, hormones, herbs, vitamins, and lifestyle choices

RECOVER Brain Function & Optimize Performance:

- More resilient, disciplined, focused, and confident leader



Lee DA, et al. Tanycytes of the hypothalamic median eminence form a diet-responsive neurogenic niche. *Nature Neuroscience* 15, 700–702 (2012) doi:10.1038/nn.3079.

Neurogenesis Repairs Brain Function and Performance

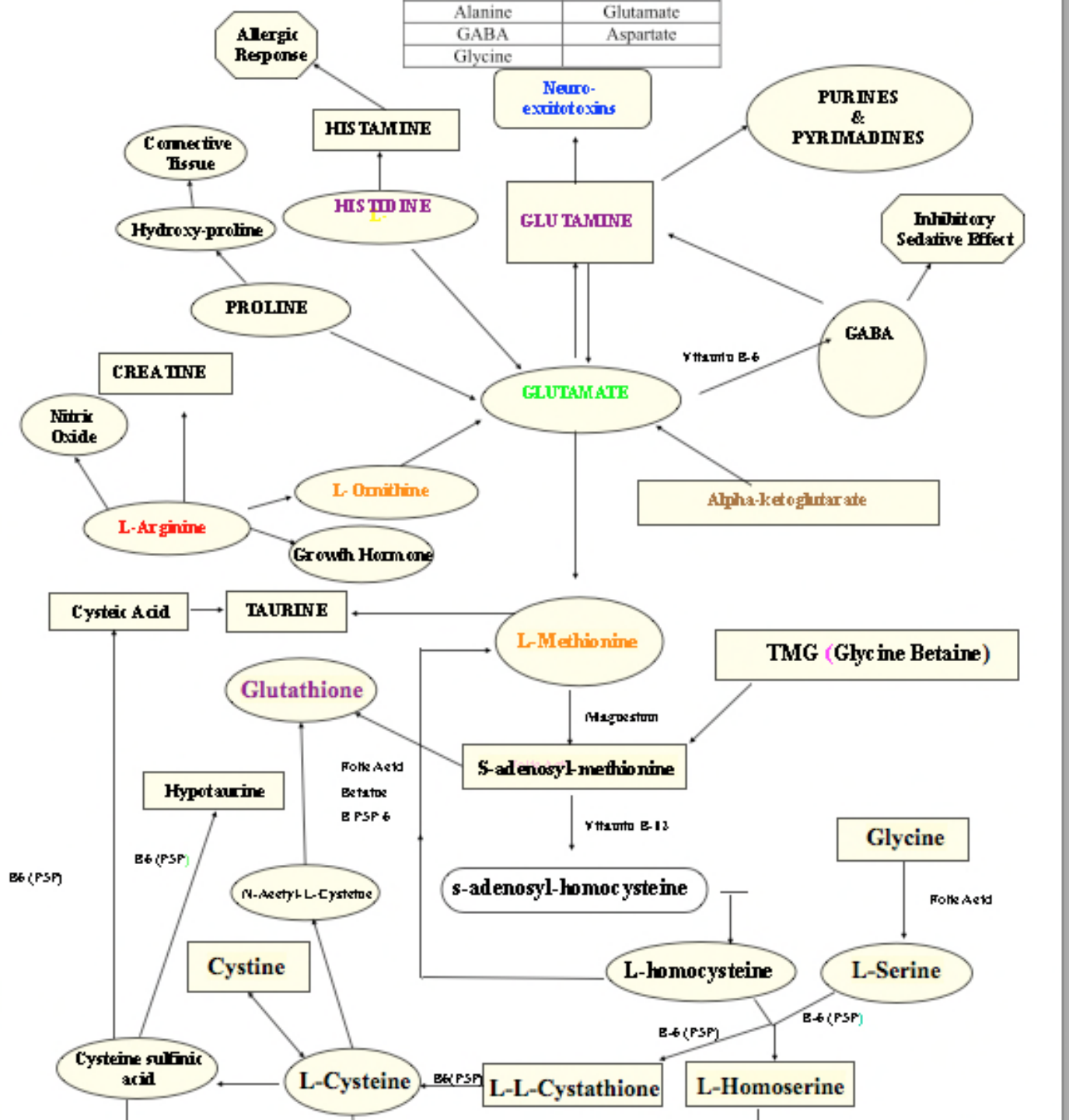
- Improves rapid visual information processing
- Enhances paired associate learning
- Regains spatial recognition
- Reverses executive problems and low IQ
- Reverses memory decline
  - Visual
  - Auditory
  - Working
  - Immediate

C. H. Salmond[1,4], D. A. Chatfield[2], D. K. Menon[1,2], J. D. Pickard[1,3] and B. J. Sahakian **Cognitive sequelae of head injury: involvement of basal forebrain and associated structures Brain Advance Access originally published online on November 17, 2004 Brain** 2005 128(1):189-200; doi:10.1093/**brain**/awh352

Conclusion

- You can reverse and delay the impact of mental and physical decline by up to 15 years through brain chemistry optimization
- Brain chemistry deficiencies and imbalances can be identified through proper brain and body testing
- Deficiencies can be addressed through a combination of brain and body repair mechanisms

End result: A smarter, faster more optimally performing brain and body


Alanine
Glutamate
GABA
Aspartate
Glycine
Allergic Response
HISTAMINE
Neuro-excitotoxins
PURINES & PYRIMADINES
Connective Tissue
HISTIDINE
GLUTAMINE
Inhibitory Sedative Effect
Hydroxy-proline
PROLINE
GABA
Vitamin B-6
CREATINE
GLUTAMATE
Nitric Oxide
L- Ornithine
Alpha-ketoglutarate
L-Arginine
Growth Hormone
Cysteic Acid
TAURINE
L-Methionine
TMG (Glycine Betaine)
Glutathione
Magnesium
Folic Acid
Betaine
B PSP 6
S-adenosyl-methionine
Hypotaurine
Vitamin B-12
Glycine
B6 (PSP)
N-Acetyl-L-Cysteine
s-adenosyl-homocysteine
Folic Acid
Cystine
L-homocysteine
L-Serine
B-6 (PSP)
B-6 (PSP)
Cysteine sulfinic acid
L-Cysteine
B6(PSP)
L-L-Cystathione
L-Homoserine