



ADHD Redefined



James Greenblatt, MD

**PSYCHIATRY
REDEFINED**

I'm Bored!



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Left untreated, debilitating symptoms of ADHD can negatively impact:

- Academic Achievement
- Self-esteem and Satisfaction
- Driving Skill
- Family and Social Life
- Relationships
- Criminal activity
- Sexual behavior
- Eating habits
- Occupational status
- Job performance

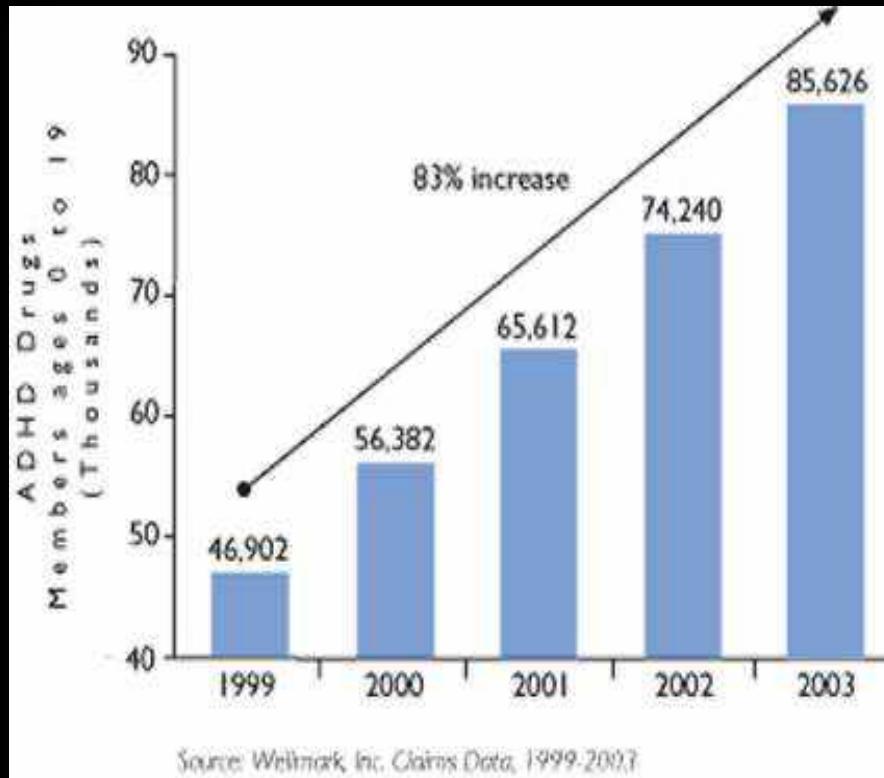
Untreated ADHD in Adolescence

Young drivers with untreated ADHD have **2-4x**
as many motor vehicle crashes as their
peers without ADHD



**Risk of totaling a car
exceeds that of a
legally drunk adult**

ADHD Medication Use



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Diary of a Young Psychiatrist

DRUGS!

NO DRUGS!



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FUNCTIONAL MEDICINE



- Biochemistry
- Lab testing
- Genetics
- G x E
- Etiology – root causes

INTEGRATIVE MEDICINE



- Diet, lifestyle, environment
- Mindfulness, spirituality
- Body-mind-spirit balance

WE NEED BOTH!

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UNIQUE INDIVIUDAL, UNIQUE BIOLOGY....

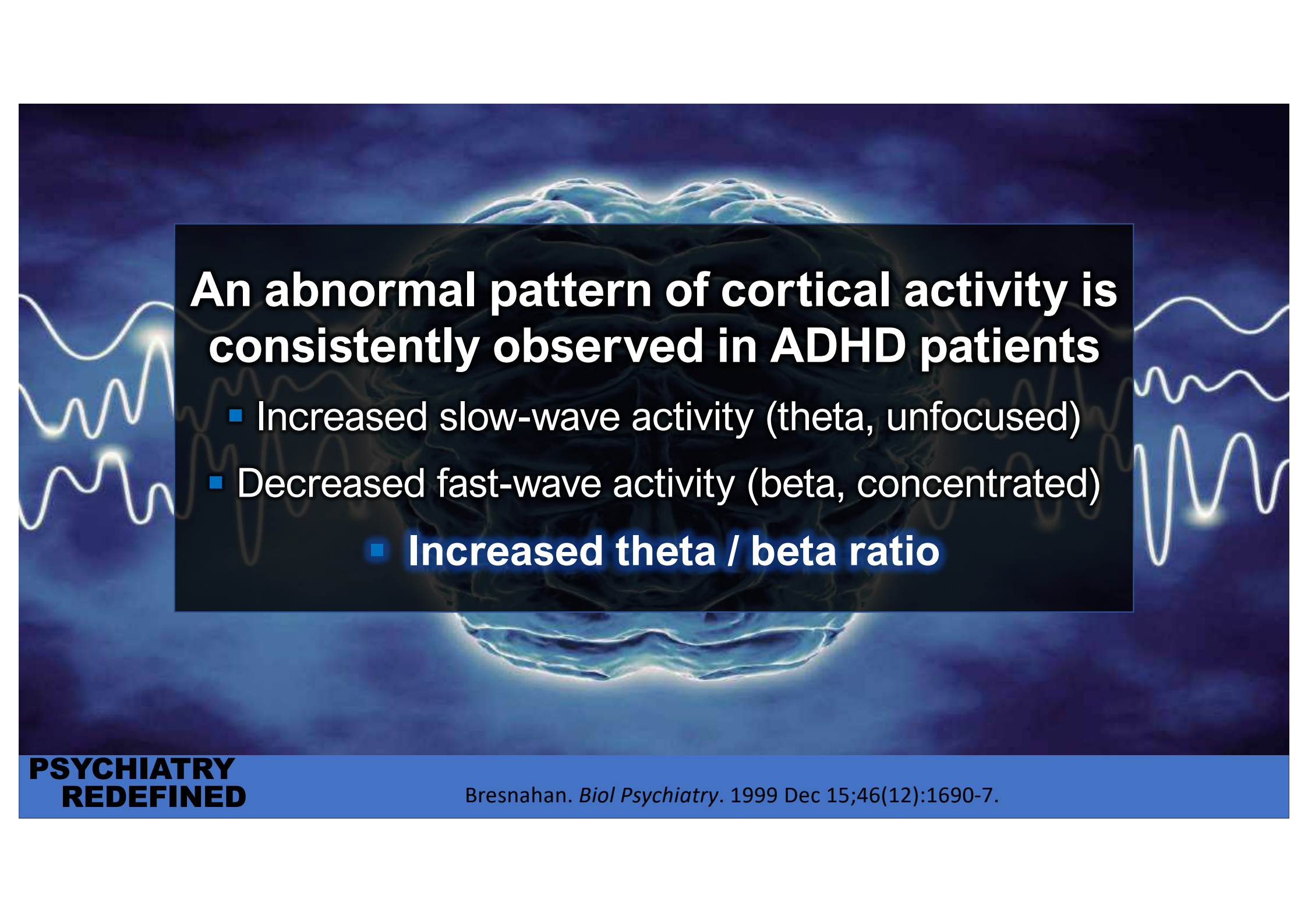


...UNIQUE DISEASE

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Brain Waves

Brain Waves	Frequency	Mental Condition
Delta wave	0.5 - 3 Hz	deep sleep
Theta wave	4 - 7 Hz	light sleep
Alpha wave	8 - 13 Hz	awake, relaxed
Beta wave	14 Hz	awake, excited



An abnormal pattern of cortical activity is consistently observed in ADHD patients

- Increased slow-wave activity (theta, unfocused)
- Decreased fast-wave activity (beta, concentrated)
 - **Increased theta / beta ratio**



Joel F. Lubar Ph.D.

Starting with studies in the 1970s, Lubar developed EEG Biofeedback (Neurofeedback) as a treatment modality for children, adolescents, and adults with ADHD.

In a 1992 publication, in *Pediatric Neurology*, it was first shown that children with the inattentive form of ADD (without hyperactivity), differ significantly in terms of quantitative EEG patterns, from matched control non-ADD children.

The American
Academy of
Pediatrics
designated
neurofeedback as
“Level 1 - Best
Support”



The highest level of support, as
an intervention for attention and
hyperactivity behavioral
problems

Neurofeedback

91 children with ADHD, mean age 10.5 years

Randomized to 30 sessions of beta/theta neurofeedback, MPH (20-60 mg/d), or both



Neurofeedback was as effective as medication

Neurofeedback

104 children aged 7-11 randomized to neurofeedback (NF), cognitive training, or a control condition over 5 months

NF group had

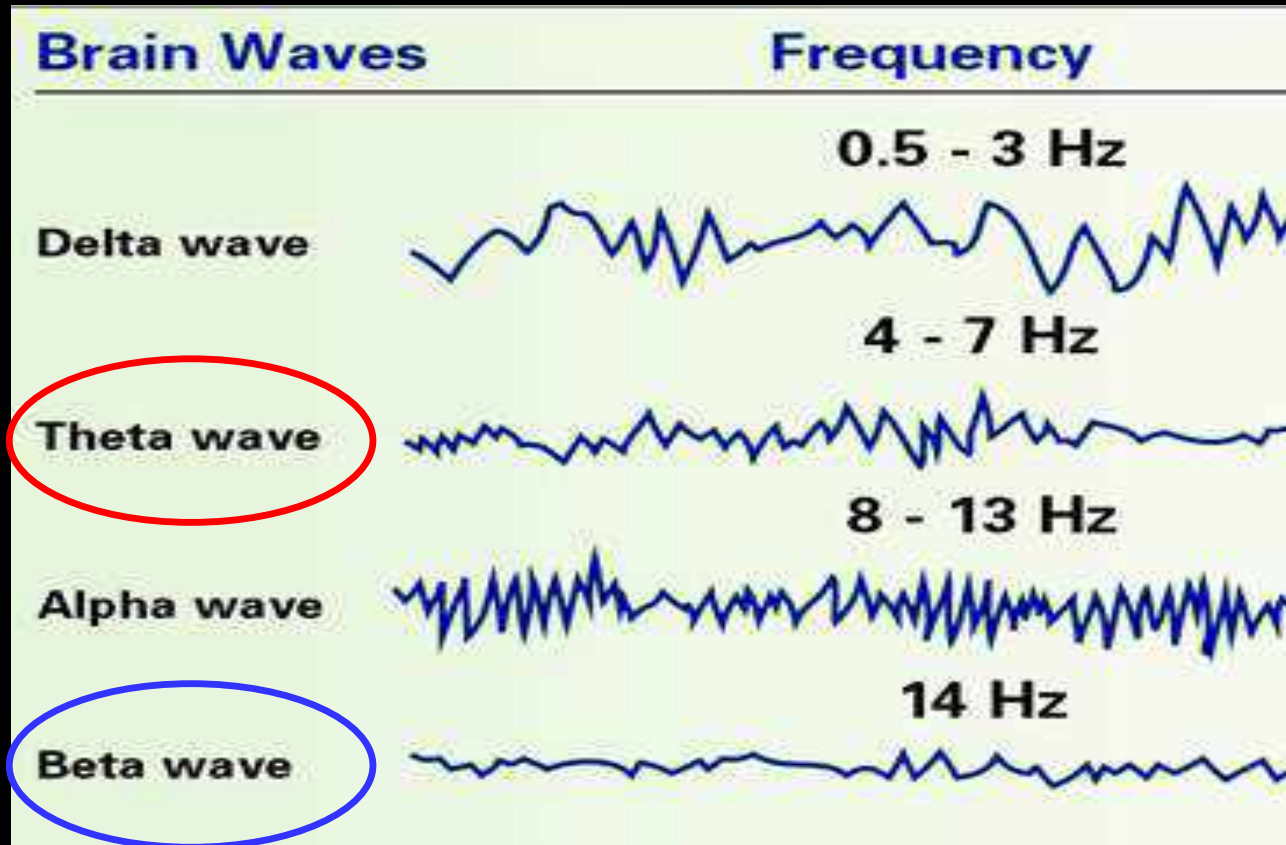
Stimulant medication

NF children had quicker & greater improvements in ADHD symptoms, which were maintained at the 6-month follow-up

behavior vs. controls

those in the NF condition

Brain Waves



**PSYCHIATRY
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DRUGS!

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OPCs

A type of polyphenol, a compound that plants produce to protect themselves from environmental harm

Oftentimes a plant pigment:

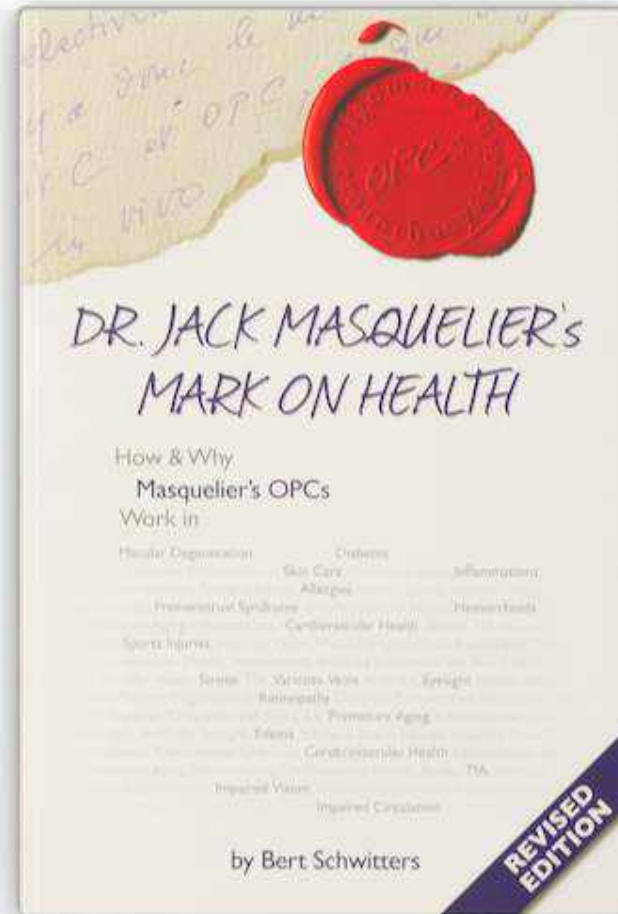
- the blue in blueberry
- the red in grapes
- the green in green tea
- the dark brown in dark chocolate

Miracle Cures

Dramatic New Scientific Discoveries Revealing the Healing Powers of Herbs, Vitamins, and Other Natural Remedies

Jean Carper

Author of the *New York Times* Bestsellers
Stop Aging Now! and *Food—Your Miracle Medicine*



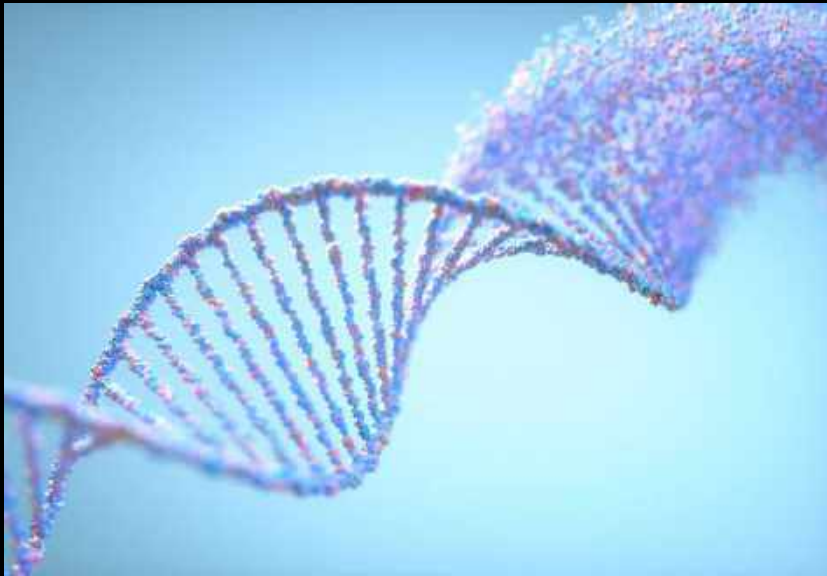
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Pycnogenol



- Phenolic extract derived from the bark of the French Maritime Pine (*P. pinaster*)
- Brand name “Pycnogenol”
- Readily crosses blood brain barrier
- Nontoxic, nonmutagenic, noncarcinogenic, and free of side effects

Pycnogenol Supplementation



- RCT on 61 children with ADHD; pycnogenol (1 mg/kg/d) or placebo
- **At baseline ADHD children had significantly increased DNA damage vs. controls**

Pycnogenol reduced DNA damage, normalized antioxidant status, and improved attention

Pycnogenol Supplementation



- RCT on 61 children with ADHD; Pyc or placebo
- **Significant reduction of hyperactivity, improved attention and visual-motor coordination, and improved concentration**

Pycnogenol Supplementation



- 53 healthy students given Pycnogenol; significantly improved sustained attention, memory, alertness, executive functions, mood
- Pyc group = higher test scores on exams vs control group
- **Levels of anxiety decreased by 17%**

Pyc improves cognitive function, attention, & mental performance

OPCs

Also found in

- red wine
- ginkgo biloba
- peanut skin
- cranberries
- plums
- peaches
- blueberries
- grape seeds





**PSYCHIATRY
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DATE 3 10 99 TIME Today

BY _____

OBSERVATION	DEGREE OF ACTIVITY			
	NOT AT ALL	JUST A LITTLE	PRETTY MUCH	VERY MUCH
1 Restless or Overactive		/		
2 Excitable, Impulsive			✓	
3 Disturbs other children			✓	✓
4 Fails to finish things he starts - Short attention span		/		✓
5 Constantly fidgeting		/	✓	
6 Inattentive, Easily distracted			✓	✓
7 Demands must be met immediately - Easily frustrated	✓			✓
8 Cries often and easily	✓			
9 Mood changes quickly and drastically	✓			
10 Temper outbursts, Explosive and unpredictable behavior	✓			
11	✓			
12				
13				
14				
15				

COMMENTS: In novel group, starts singing & making faces while other students are talking.

DATE 4 9 99
Month Day Year

TIME FRI

BY _____

	OBSERVATION	DEGREE OF ACTIVITY			
		NOT AT ALL	JUST A LITTLE	PRETTY MUCH	VERY MUCH
1	Restless or Overactive	PM ✓		AM ✓	
2	Excitable, Impulsive		PM ✓	" ✓	
3	Disturbs other children	✓		" ✓	
4	Fails to finish things he starts - Short attention span	PM ✓		AM ✓	
5	Constantly fidgeting				✓
6	Inattentive, Easily distracted		✓		
7	Demands must be met immediately - Easily frustrated	✓			
8	Cries often and easily	✓			
9	Mood changes quickly and drastically	✓			
10	Temper outbursts, Explosive and unpredictable behavior	✓			
11		✓			
12					
13					
14					
15					

COMMENTS: Sam came into school keyed up. The morning was difficult. By afternoon he calmed down & maintained focus. The accompanying note was what he wrote at recess. I left the room for an ed plan meeting for 1/2 hour in the AM Sam went to the bathroom for 15 minutes, then fiddled around ^{too} much during the time I was out

DATE 5 4 99
Month Day Year

TIME Tuesday up to 1:30 BY _____

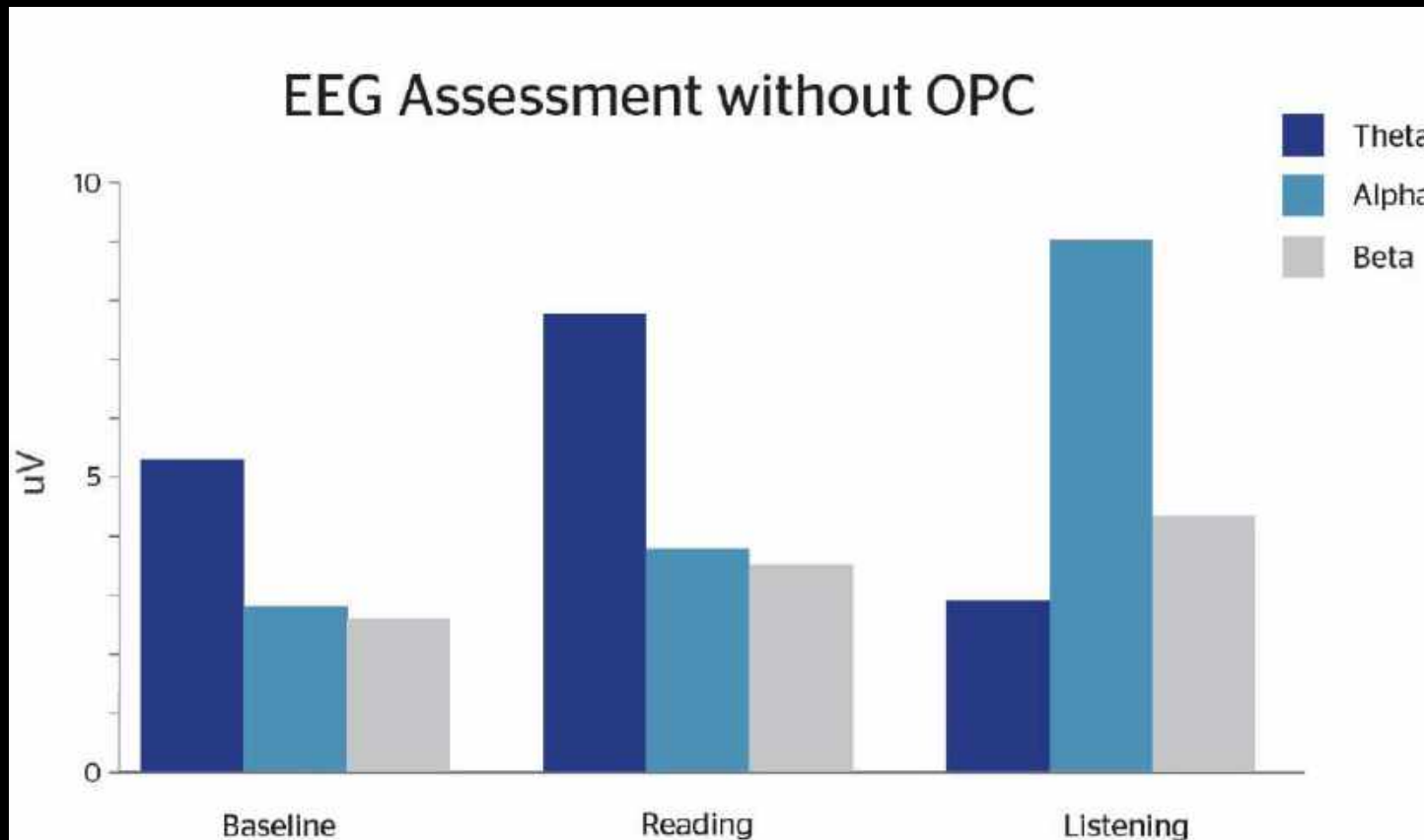
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9	Mood changes quickly and drastically	✓			
10	Temper outbursts, Explosive and unpredictable behavior	✓			
11					
12					
13					
14					
15					

COMMENTS: ! what can I say!
Sam had a quiet, focused, hardworking day.

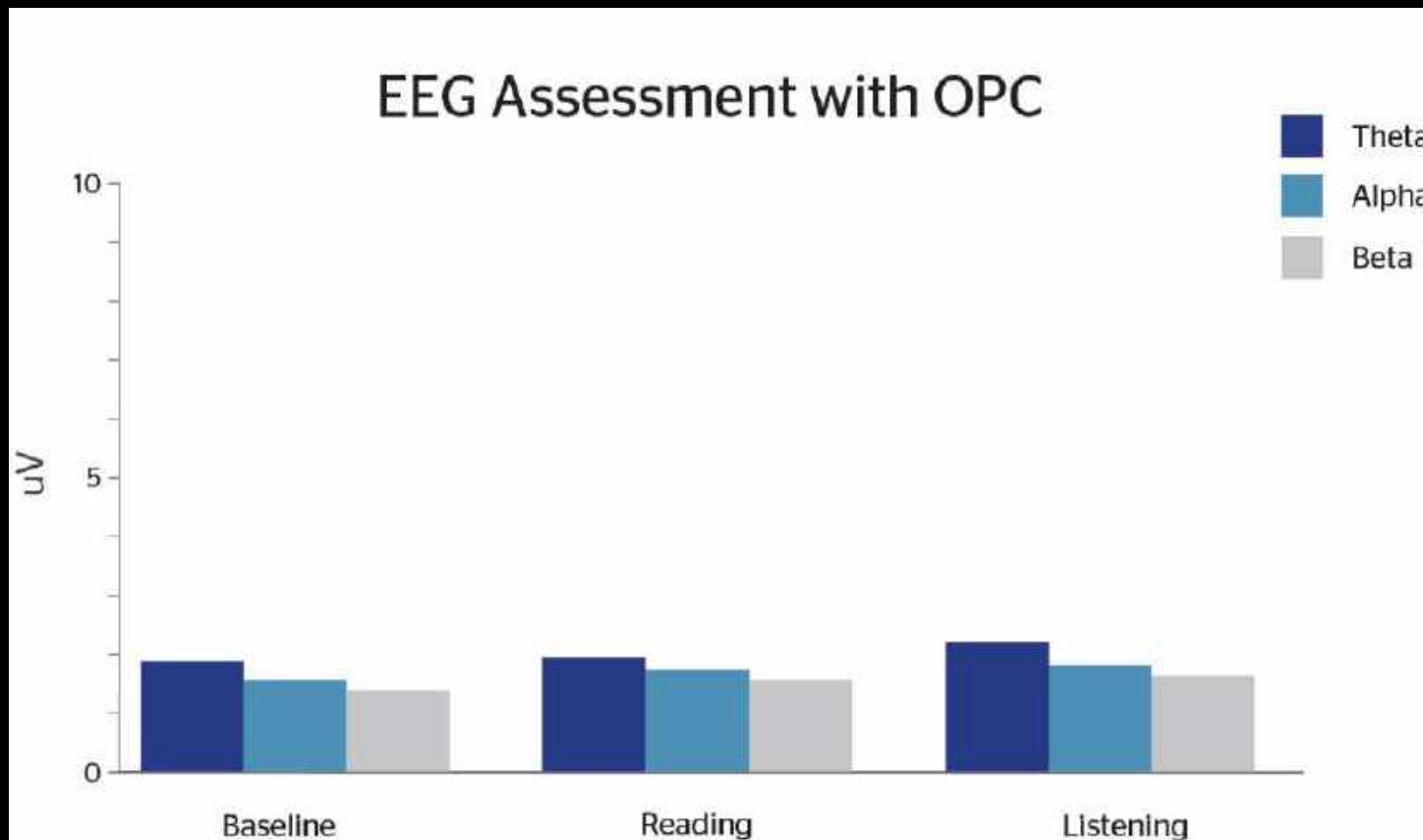
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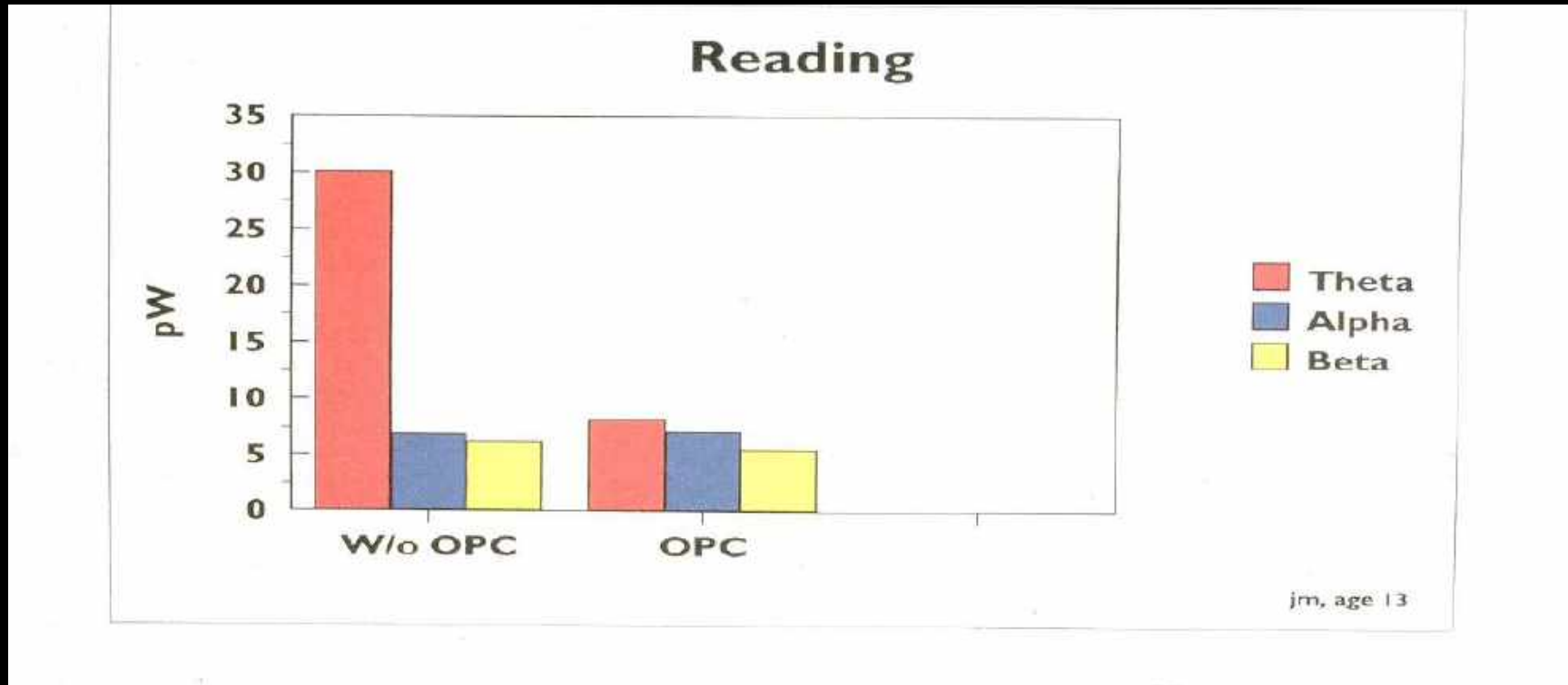
OPCs



OPCs

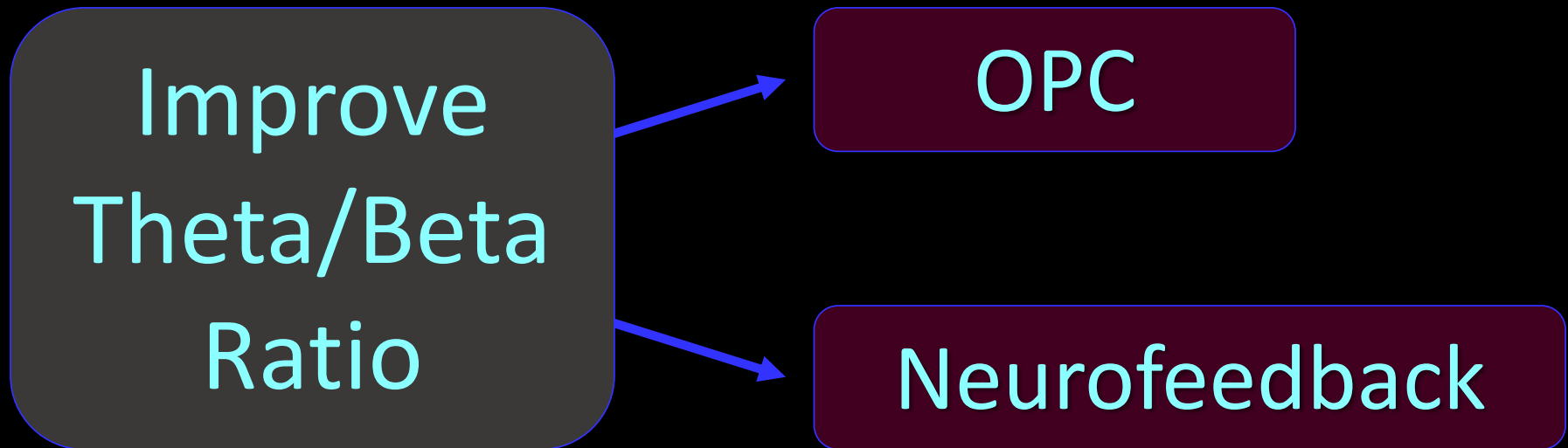


OPCs



Theta/Beta Ratios

The theta/beta ratio has been shown to be predictive of a diagnosis across the lifespan



OPCs Improve Brain Function

Double-blind RCT with 26 adults, mean age 68 years

Consumed either 30ml blueberry concentrate (providing 387 mg anthocyanidins) or placebo 1x/day for 12 weeks

Pre- and post-baseline, subjects completed cognitive testing battery in fMRI



Significant increases in brain activity and gray matter perfusion were observed in the OPC group, along with working memory improvements

General benefits of OPCs

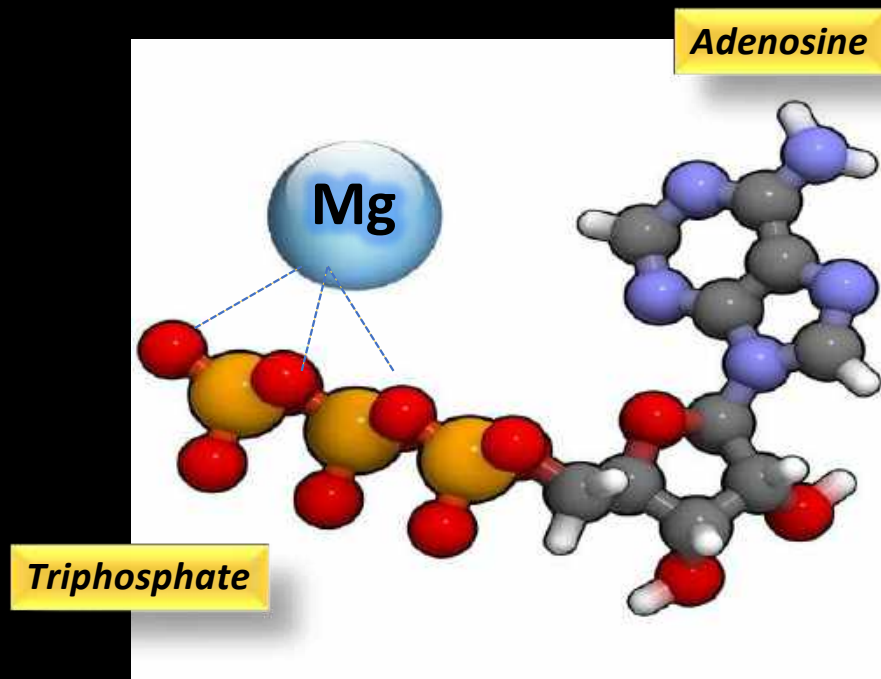
- Strengthens veins and capillaries
- Improves circulation
 - Reduces diabetic retinopathy
- Smooth and elastic skin
- Improves joint flexibility
 - Fights inflammation
- Slows cell mutagenesis
- Prevents ulcer formation
 - Reduces allergies

Properties	Biochemical Action	Implications for Health
Balance brain waves	Improve theta : beta brain wave ratio	Improve attention & focus
Normalize mineral balance	Chelate copper, improving copper : zinc ratio	Reduce irritability, agitation; improved SER, DOPA synthesis
Antihistamine / anti-inflammatory	Modulate inflammatory pathways; slow histamine synthesis & release	Reduce neuro-inflammation, modulate immune hyperactivity
Strengthen / repair blood-brain barrier	Maintain integrity of tight junctions, strengthen blood vessels	Protect the brain from proinflammatory molecules; mitigate “leaky brain”
Antioxidant properties	Destroy free radicals, lower levels of oxidative stress	Reduce cell damage
Stimulate BDNF expression & activity	Increase BDNF expression + activity in neural tissues	Promote neurogenesis, neurorestoration, neuroplasticity



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Magnesium



Mg is part of the structure of ATP

- 4th most abundant mineral in the body
- 2nd most prevalent mineral cells
- Highest levels found in the brain and heart

Symptoms of Magnesium Deficiency

Poor
concentration

Irritability

Anxiety



Mood lability

Sleep
dysfunction

Depression,
apathy

Magnesium Depletion

- ✓ Medications
- ✓ Alcohol
- ✓ Caffeine
- ✓ Soft drinks
- ✓ Stress

All Deplete Mg



Medications Drain Magnesium

Stimulant drugs like Ritalin and Adderall *leach magnesium from the body*

A deficiency of magnesium is often behind ADHD drug side effects like irritability, agitation, anxiety, insomnia, facial tics, and nail biting



Magnesium and ADHD

Magnesium deficiency occurs more frequently in children with ADHD

116 children (94 boys & 20 girls) aged 9-12 with ADHD

- **Magnesium deficiency was found in 95%** of those examined

Magnesium & ADHD

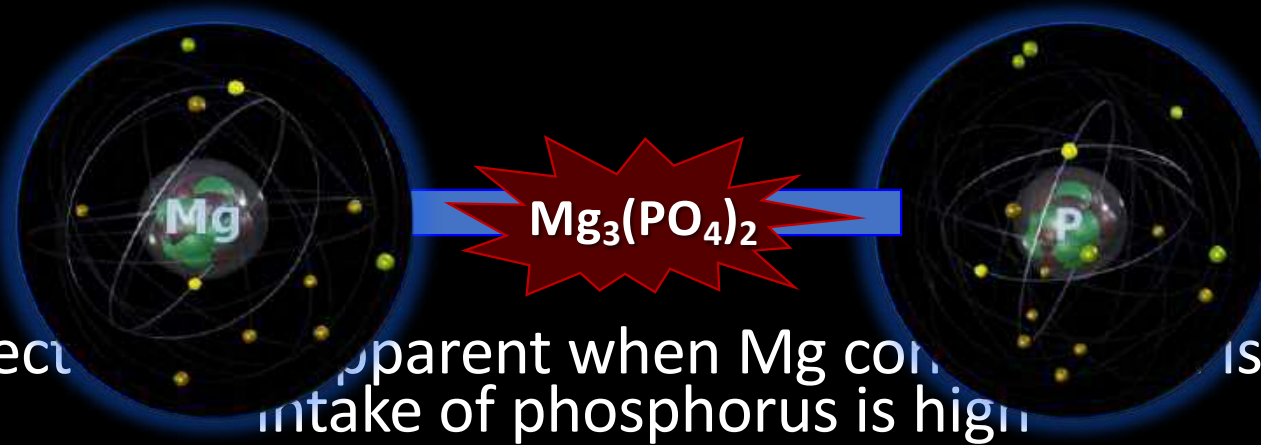
- 20 ADHD children, 20 controls
- **Children with ADHD:** significantly lower levels of serum Mg; 65% Mg deficient



Significant correlation between hair Mg levels and inattention, hyperactivity, impulsivity

Magnesium & Phosphorus

In the GI tract, phosphorus and Mg form a complex, and render each other unavailable for absorption



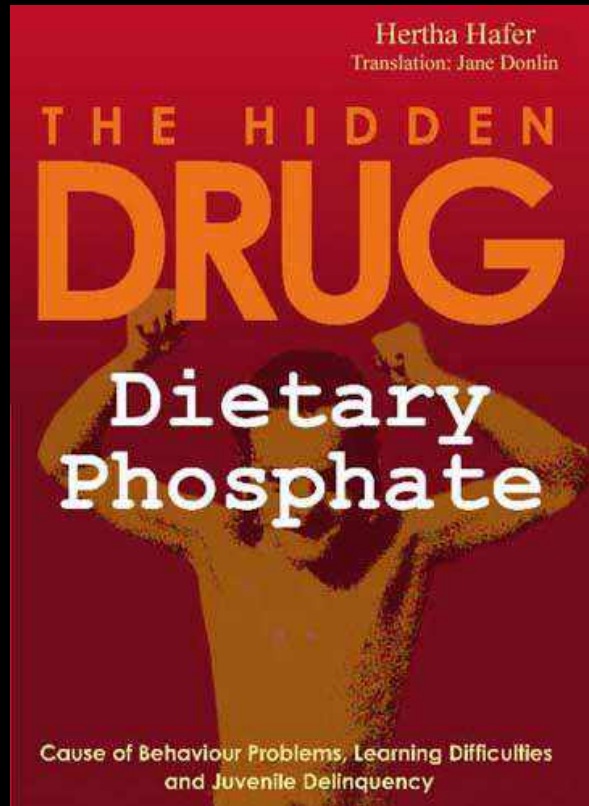
This effect is most apparent when Mg concentration is low and intake of phosphorus is high

Scientific Support

- Men drank 3 quarts of cola per day for two consecutive days
- Serum + 24-hour urine samples obtained
- After consumption, **serum phosphate levels increased** in 75% of subjects and associated with **significant decreases of Mg excretion**



Phosphate & ADHD



Hertha Hafer, a German pharmacist, suggests a low phosphate diet as a treatment for ADHD in *The Hidden Drug, Dietary Phosphate: Cause of Behavior Problems, Learning Difficulties and Juvenile Delinquency*

Magnesium Clinical Pearls

- Hard to detect in laboratory testing
- RBC magnesium helpful
- Hair test helpful – Ca/Mg ratios

Constipation

Irritability

Anxiety

Insomnia

Clinical Symptoms

Selecting the ideal magnesium product

125-300 mg magnesium glycinate per meal and at bedtime provides clinically significant mood benefits

200-300 mg magnesium glycinate or citrate before bed supports sleep onset and duration through the night

Magnesium (citrate)

Magnesium (aspartate)

Magnesium (glycinate)

Magnesium (threonate)

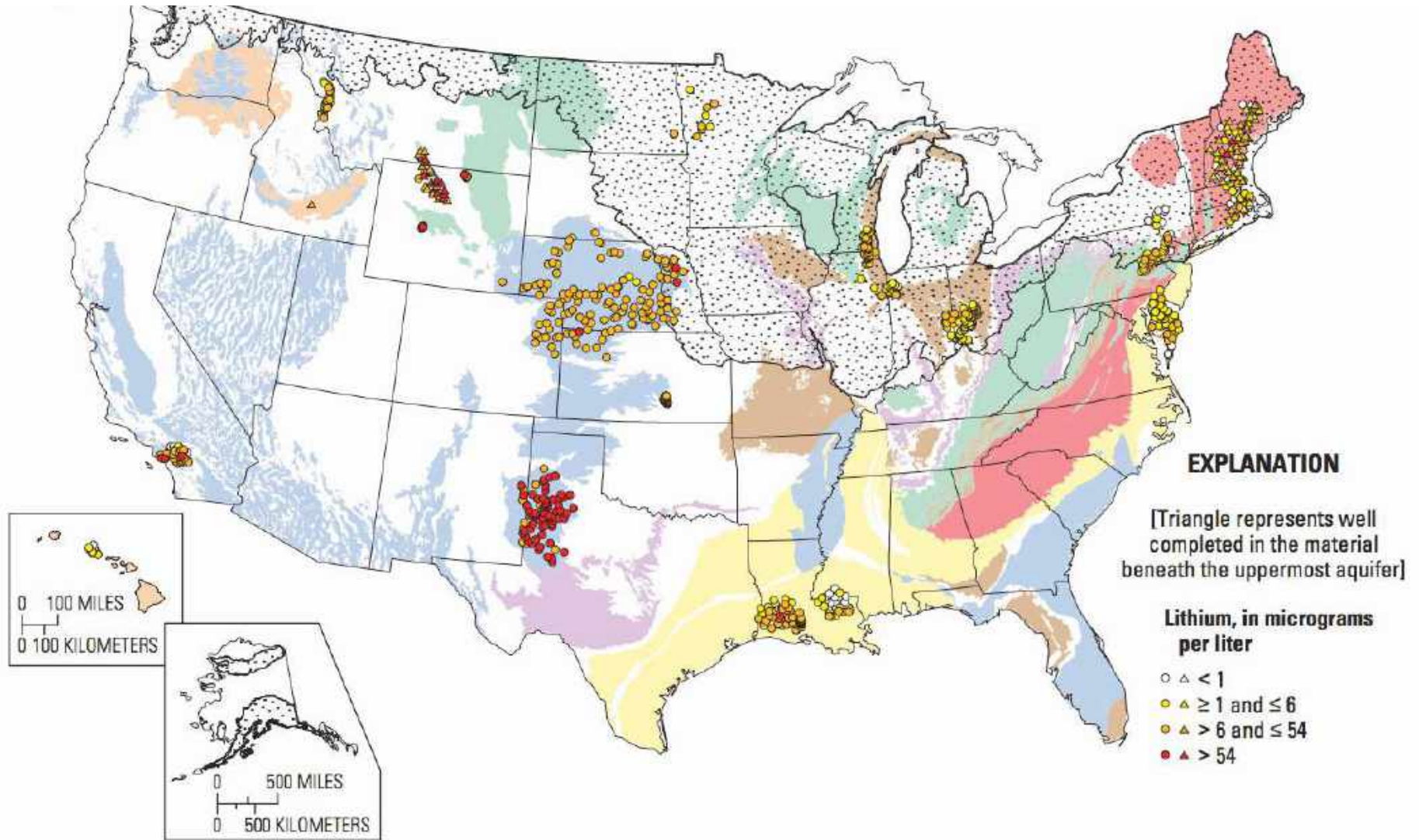
~~Magnesium (oxide)~~



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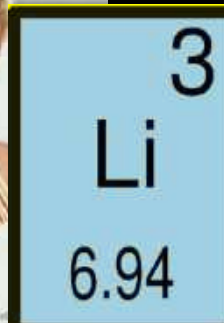


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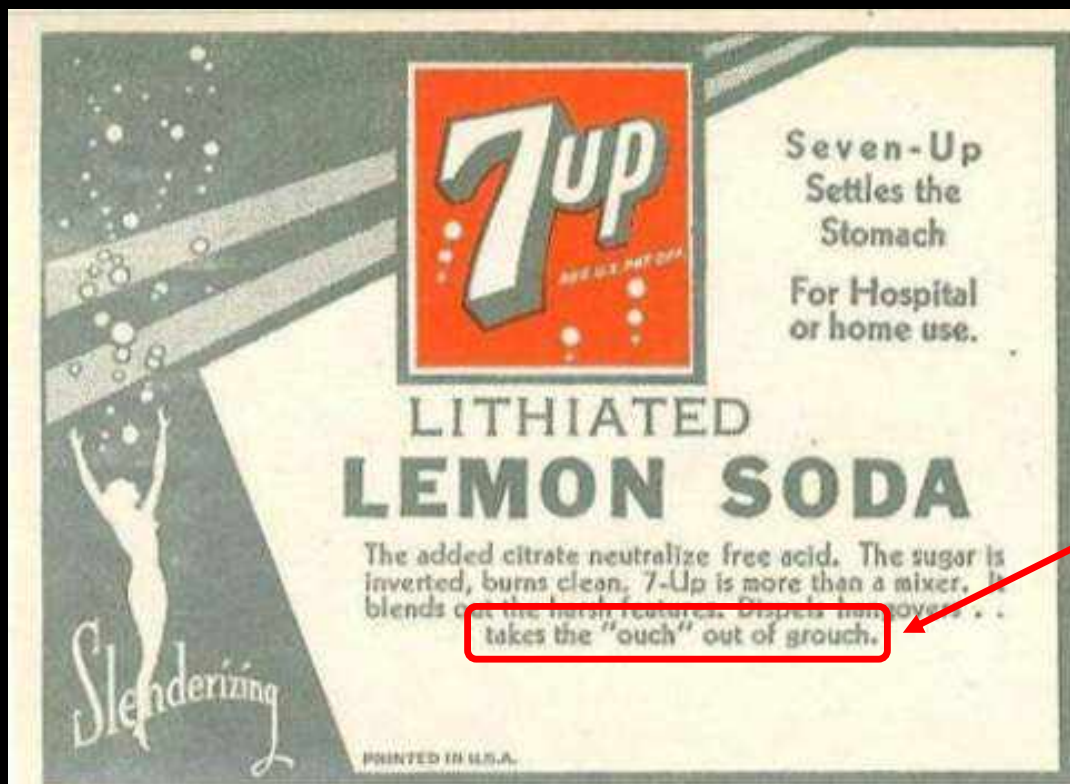
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U.S. Department of Geological Survey - National Water-Quality Assessment Program: 2011



7 Up contained lithium citrate from 1929 until 1950

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“Takes the ‘ouch’ out of ‘grouch’”



**PSYCHIATRY
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“Irritability is everywhere and nowhere at once”



**NO reliable
marker,
measure, or
test to diagnose**



**NO set of
established
diagnostic
criteria**



**NO
TREATMENT**

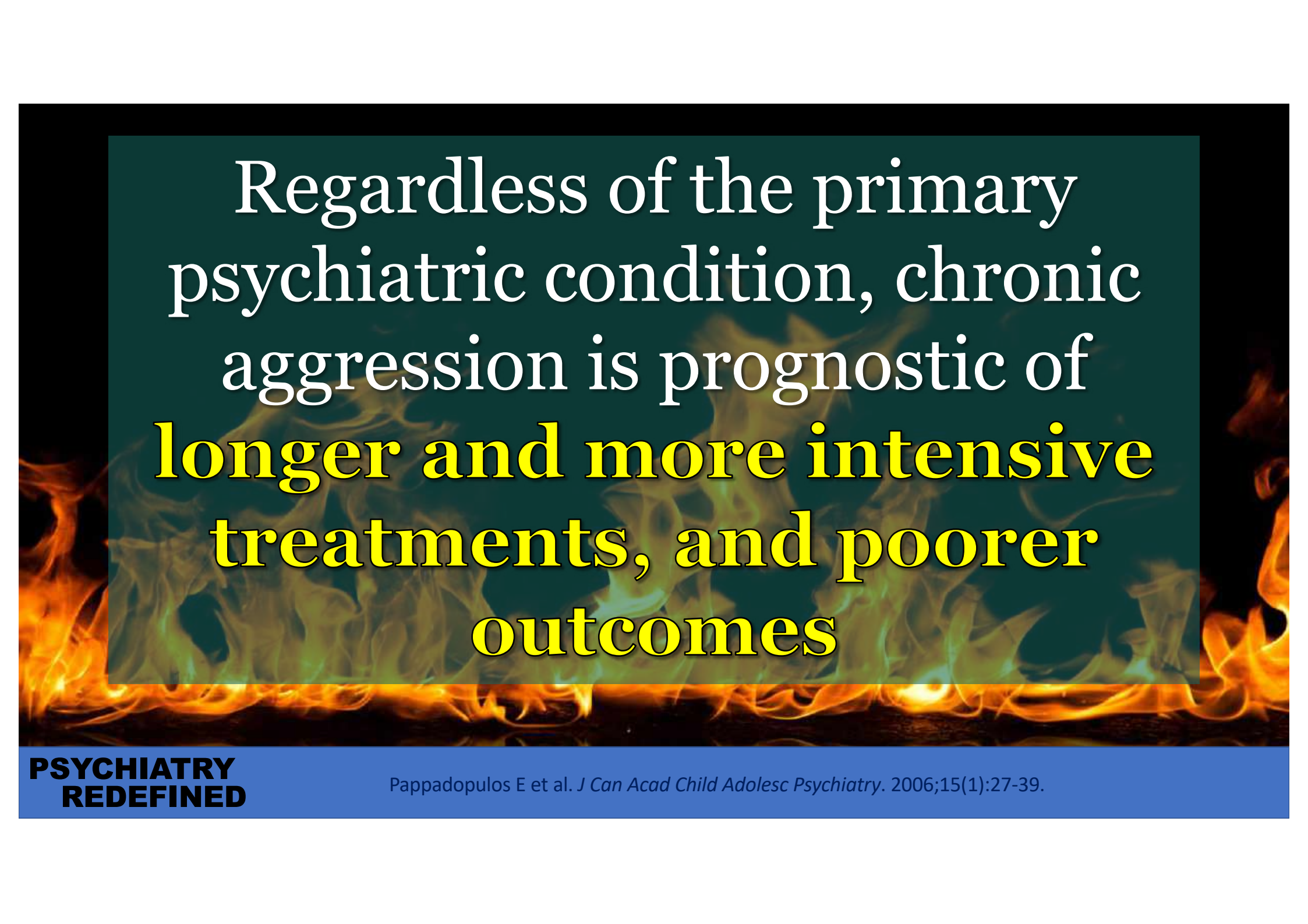
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Association of Childhood Irritability and Depressive/Anxious Mood Profiles With Adolescent Suicidal Risk

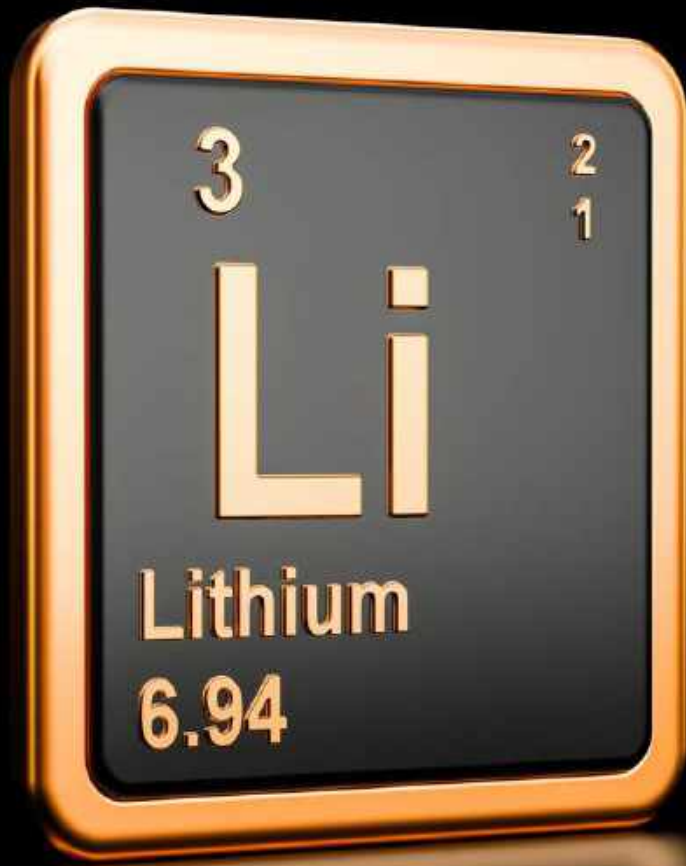
- ◆ 1,430 participants
- ◆ Yearly or bi-yearly assessments
- ◆ Outcomes: suicidal ideation (self-report)

Early manifestation of chronic irritability during childhood, especially when combined with depressive/anxious mood, may be associated with an elevated risk for adolescent suicidality.

Children with high irritability and depressive/anxious mood and, to a lesser extent, with moderate irritability only had a higher suicidal risk during adolescence vs. children with low symptom levels.



Regardless of the primary psychiatric condition, chronic aggression is prognostic of **longer and more intensive treatments, and poorer outcomes**



When is low-dose lithium the appropriate solution?

Therapeutic Applications of Low-Dose Lithium

ADHD

DMDD

Conduct
Disorder

Substance
Use Disorder



Mood Disorders

- *Depression with irritability*

Bipolar II

Autism

Alzheimer's
with irritability

DIAGNOSTIC AND STATISTICAL
MANUAL OF
MENTAL DISORDERS
FIFTH EDITION

DSM-5

AMERICAN PSYCHIATRIC ASSOCIATION

Disruptive Mood
Dysregulation
Disorder
(DMDD)

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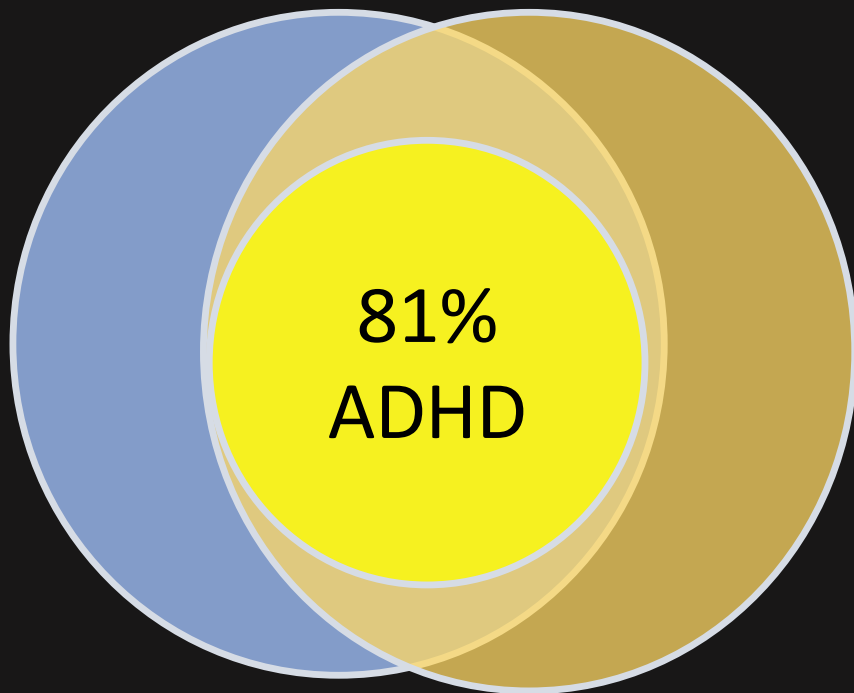
Disruptive Mood Dysregulation Disorder



Severe recurrent temper outbursts manifested verbally and/or behaviorally that are not appropriate for the situation

The mood between temper outbursts is persistently irritable

DMDD Prevalence, Comorbidity and Correlates



- Mental health center sample of 597 youths: 31% met DMDD criteria
- DMDD youth significantly more likely to have comorbid dx of ODD, CD, and ADHD vs non-DMDD youth

In DMDD youth, 96% met criteria for ODD, 81% ADHD, and 24% CD

Persistence of DMDD in children with ADHD



20–30% of children with ADHD have comorbid DMDD

DMDD highly transient in children with ADHD, but a subset experience chronic comorbidity

Treatment Options for DMDD

No established guidelines

Pharmacotherapeutic options for aggression and chronic irritability:

- Antidepressants/SNRIs
 - Mood stabilizers
 - Psychostimulants
 - Antipsychotics
 - Alpha-2 agonists

Treatment for DMDD: Review

- 8 completed studies, 7 ongoing; 4 completed, 3 ongoing psychopharmacy
- Possible efficacy of psychotherapy, only 2 main psychopharmacy strategies tested



Few studies, short trial duration, no placebo, and restrictive inclusion criteria in most controlled trials

I'm Bored!

I'm Sorry!



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Lithium in Tap Water and Adolescent Aggression

- 3,040 Japanese students age 12-15
- Lithium levels measured in the schools' drinking water

Higher lithium water levels associated with:

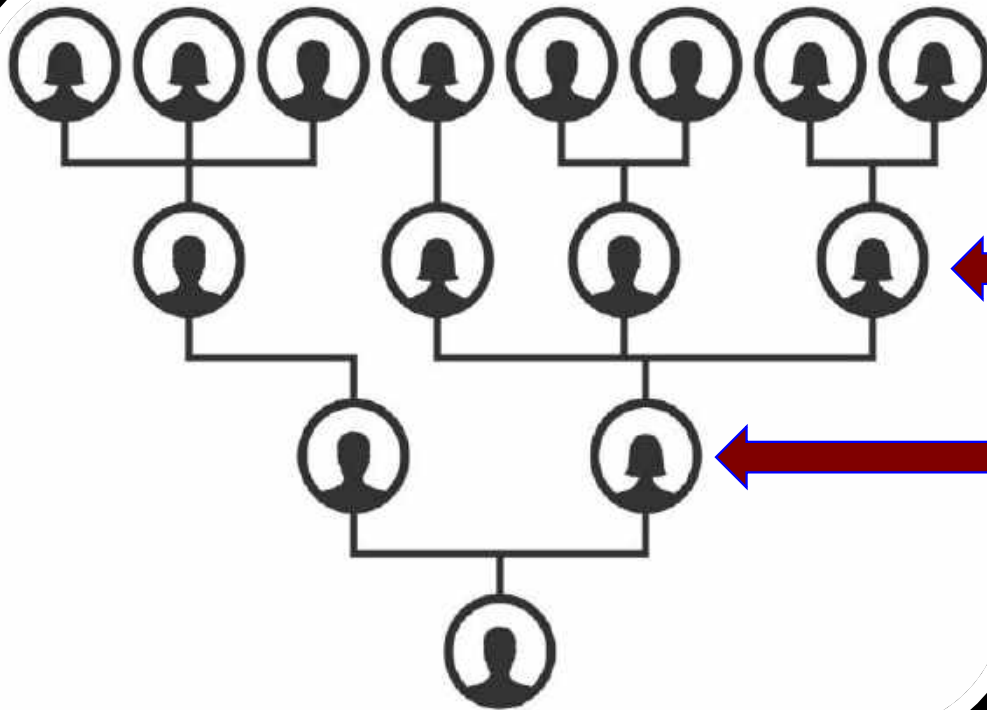
- ↓ depression symptoms
- ↓ interpersonal violence





How to decide
when to
prescribe low-
dose lithium?

TAKE A FAMILY HISTORY!!!



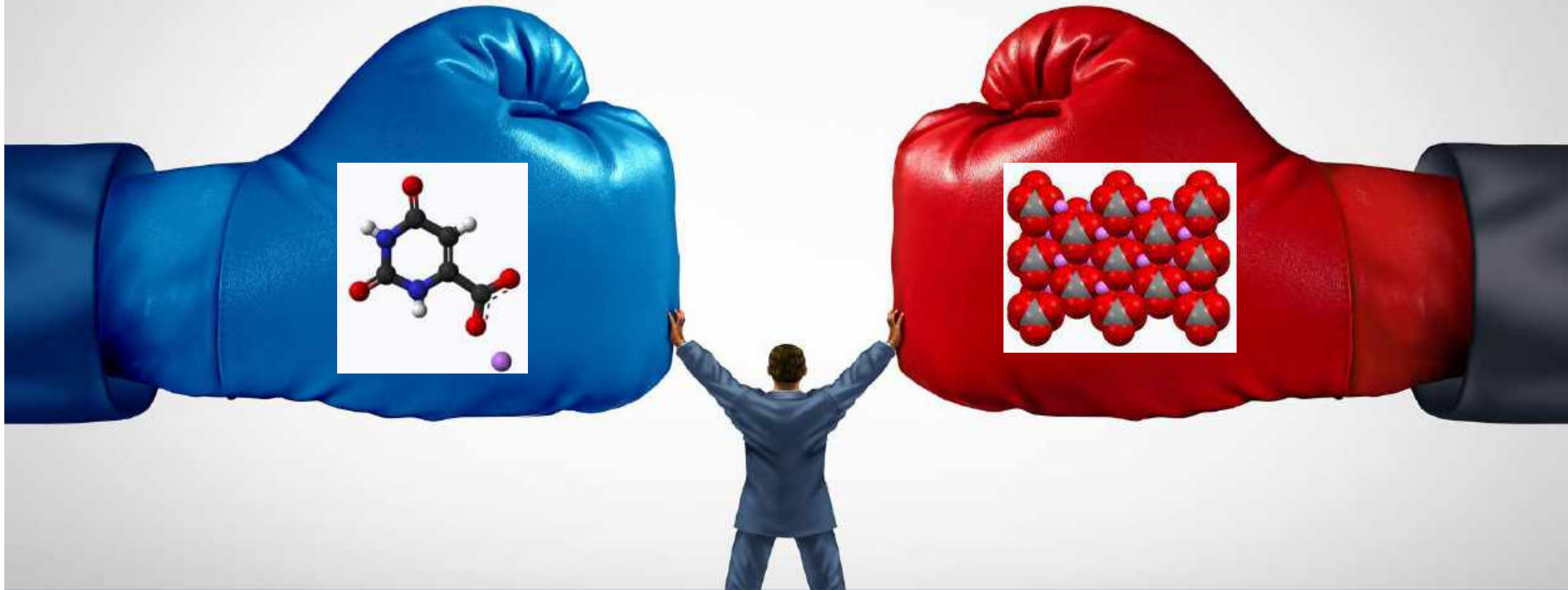
**GO BACK AT
LEAST *3*
GENERATIONS!!**

Case MK 12 y/o male: HAIR TESTING

ESSENTIAL AND OTHER ELEMENTS								
		RESULT µg/g	REFERENCE INTERVAL	PERCENTILE				
				2.5 th	16 th	50 th	84 th	97.5 th
Calcium	(Ca)	569	200- 700					
Magnesium	(Mg)	24	18- 70					
Sodium	(Na)	57	20- 200					
Potassium	(K)	82	9- 80					
Copper	(Cu)	18	11- 32					
Zinc	(Zn)	170	150- 230					
Manganese	(Mn)	0.30	0.08- 0.50					
Chromium	(Cr)	0.38	0.40- 0.70					
Vanadium	(V)	0.029	0.020- 0.075					
Molybdenum	(Mo)	0.019	0.030- 0.060					
Boron	(B)	0.75	0.34- 3.0					
Iodine	(I)	1.1	0.25- 1.3					
Lithium	(Li)	< 0.004	0.007- 0.020					
Phosphorus	(P)	180	150- 220					
Selenium	(Se)	0.64	0.70- 1.2					
Strontium	(Sr)	2.0	0.30- 3.2					
Sulfur	(S)	40400	44000- 50000					
Cobalt	(Co)	0.004	0.004- 0.020					
Iron	(Fe)	6.2	7.0- 16					

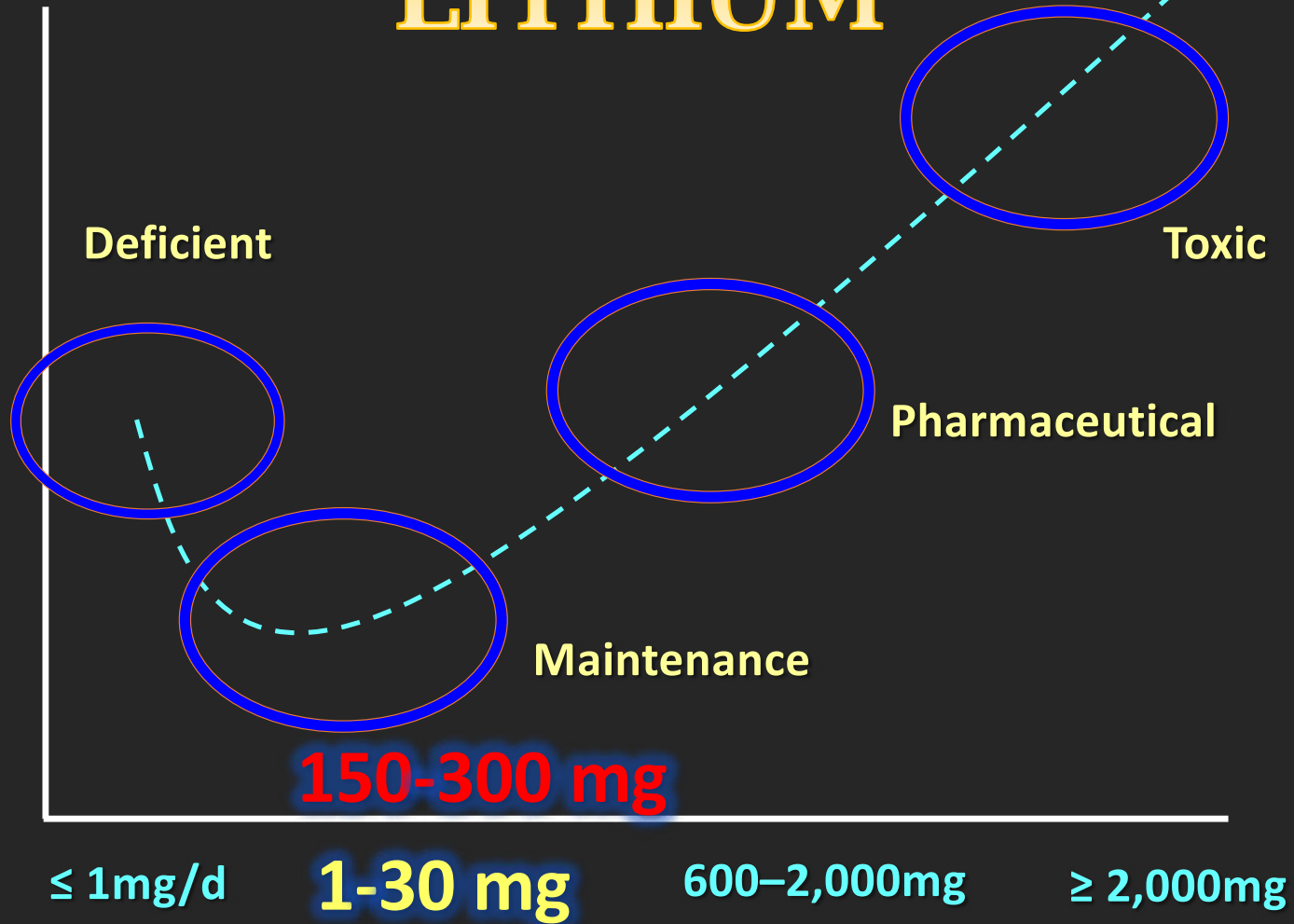


Lithium Carbonate vs. Lithium Orotate



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LITHIUM

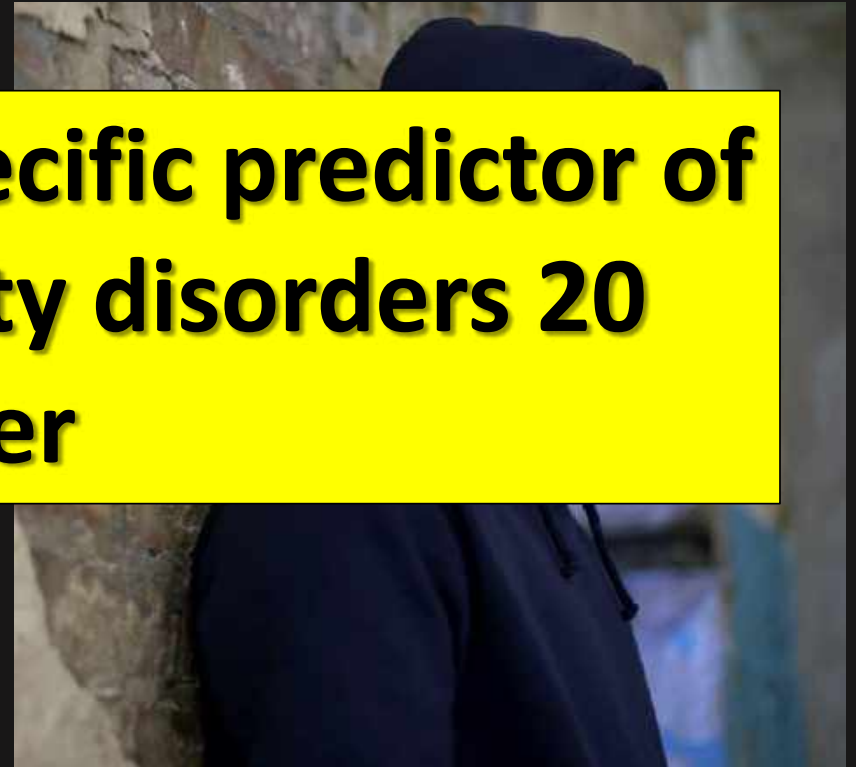


Untreated Irritability

631 participants assessed at age

1
A
W
Youth irritability is a specific predictor of depressive and anxiety disorders 20 years later

- 33x higher odds of MDD
- 72x higher odds of GAD
- 81x higher odds of dysthymia





1990

27 Texas

99 Austrian

2011

2019

15 Alabama

Japanese
municipalities

2016

2017

9 cities in
Lithuania

34
prefectures
Greece

2013

2015

145 sites
in Italy

3
ese
es

2016

274 Japanese
municipalities

2015

municipalities

counties

2013

2013

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Low-Dose Lithium

The Mineral as Medicine

An International Online Symposium

SPEAKERS:

Julie Andersen, PhD

De-Maw Chuang, PhD

John Endres, ND

Sudhir Gadh, MD

Orestis Giotakos, MD, MSc,
PhD

James Greenblatt, MD

Eric Jakobsson, PhD

Prof. Anjum Memon,
MBBS, DPhil [Oxon],
FFPH

James Phelps, MD

Event recordings & materials now available for purchase!



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