

PSYCHOPATHOLOGY II

John Gabrieli

9.00

PSYCHOPATHOLOGY

- **TREATMENT**
- **DEPRESSION (film)**
- **ATTENTION DEFICIT
HYPERACTIVITY DISORDER
(ADHD) (film)**

TREATMENT

- **Behavioral Therapy (Psychotherapy)**
 - Psychoanalysis**
 - Cognitive Behavioral Therapy (CBT)**
- **Psychopharmacology**

Psychological Therapy

Psychotherapy is a social interaction in which a trained professional tries to help another person behave and feel differently.

Who Provides Psychotherapy?

Image of telephone directory pages removed due to copyright restrictions.

Includes listing headings for Psychics, Psychoanalysts, Psychologists, and Psychotherapists.

Psychiatrist



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Psychoanalyst



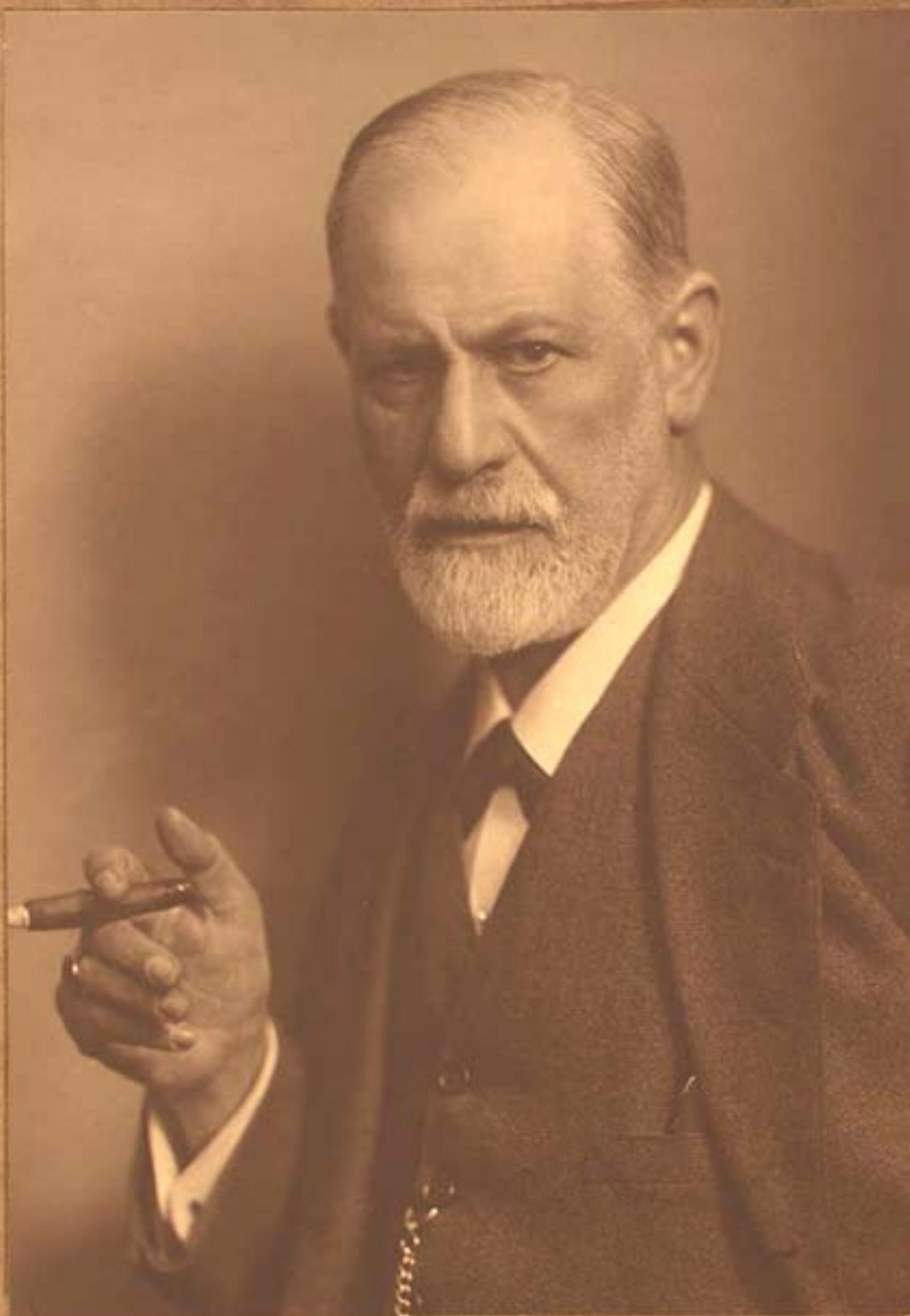
Courtesy of the Freud Museum, Vienna. Used with permission.

Freud & his couch, 1932

Other sources of psychotherapy

- **Clinical Psychologist**
- **Counseling Psychologist**
- **Clinical Social Worker**
- **Clergy**
- **Peer Groups (e.g. AA)**
- **Self-help**

**Sigmund
Freud**
(1856-1939)



Public domain image
(1921, photo by
Max Halberstadt)

Types of Psychotherapy

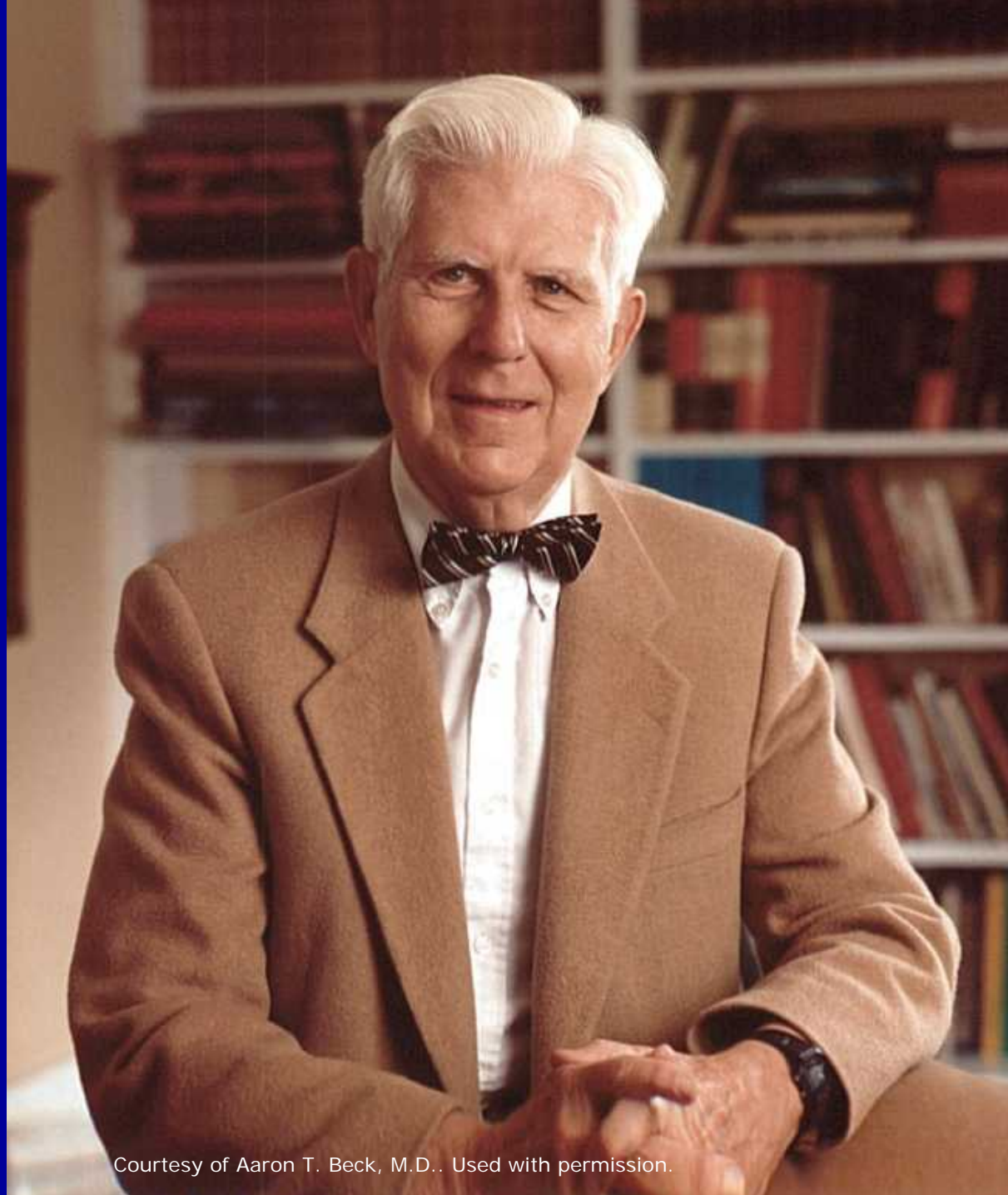
- **Psychodynamic**
 - Free association
 - Resistance
 - Transference
 - Interpretation
 - Corrective emotional experience

Aaron Beck

Born 1921

COGNITIVE BEHAVIORAL THERAPY - CBT

- Dysfunctional beliefs
- Logical errors in thinking maintain beliefs
- Focus on current problems; strategies to help
- Time-limited



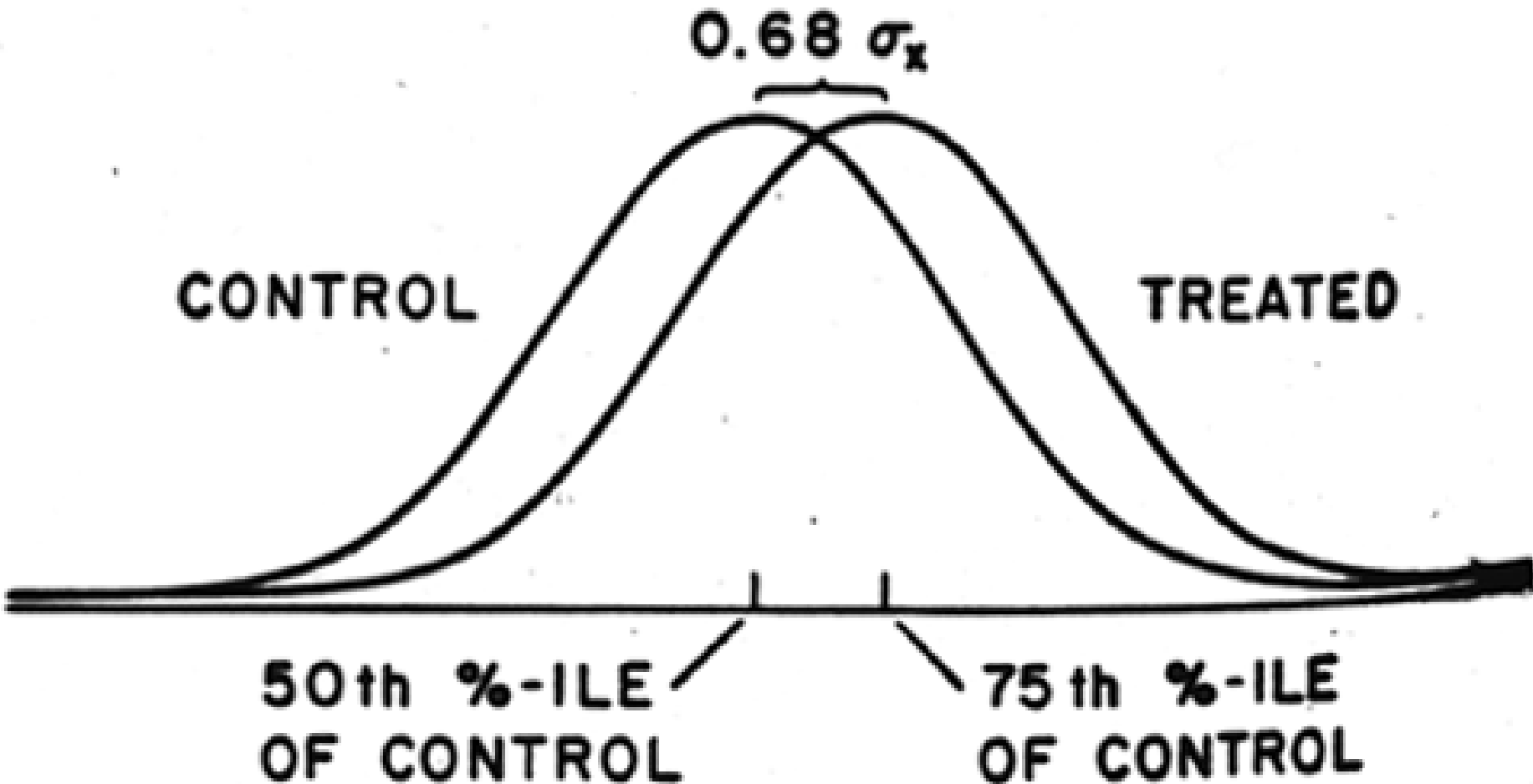
Courtesy of Aaron T. Beck, M.D.. Used with permission.

Does Psychotherapy Work?

- Initial pessimism
(Eysenck 1952)
- Cautious optimism
(Smith, Glass, & Miller, 1980)

Meta-Analysis

- Quantitative method for averaging results of a large number of different studies.
- Unit of analysis is the **effect size**, arrived at by subtracting the mean of the control group from the mean of the treatment group and dividing that difference by the standard deviation of the control group.
- The larger the effect size, the greater the effect of therapy.



AVE. EFFECT SIZE: 0.68 σ_x

STD. DEV. OF EFFECT SIZE: 0.67 σ_x

Meta-Analysis of Psychotherapy Effectiveness

(Smith, Glass, & Miller, 1980)

- The average person (50th %ile) receiving psychotherapy was better off than 80% of the persons who did not receive therapy.
- Only about 10% of effect sizes were negative → deterioration due to psychotherapy was infrequent.
- Different types of therapy were equally effective, but some advantage to cognitive and behavioral therapies.

WHEN DOES PSYCHOTHERAPY WORK?

Random assignment

Psychotherapy

Wait-list

Blind and double-blind

Meta-analysis of good efficacy of psychotherapy studies

- **2:1 chance of improvement vs. control**
- **Credentials (Ph.D., M.D., no degree) did not matter**
- **Experience of therapist did not matter**
- **Type of therapy did not matter**
- **Length of therapy did not matter**

Table removed due to copyright restrictions.

Twelve current psychiatric medications (e.g. Zoloft, Paxil, Depakote): photo of pill, how it works, side effects, and testing/approval status.

See *Time* Magazine, Dec. 8, 2003.

Cover: "[Are We Giving Kids Too Many Drugs?](#)"

Story: "[Medicating Young Minds](#)"

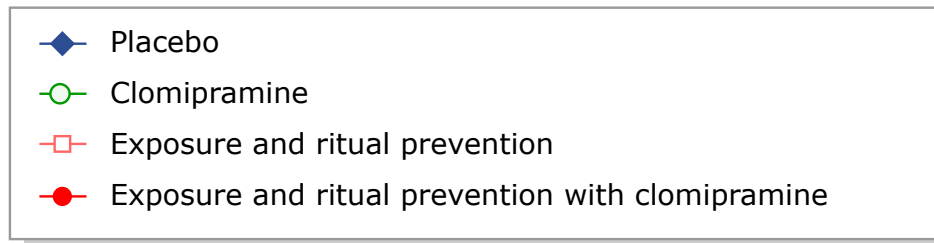
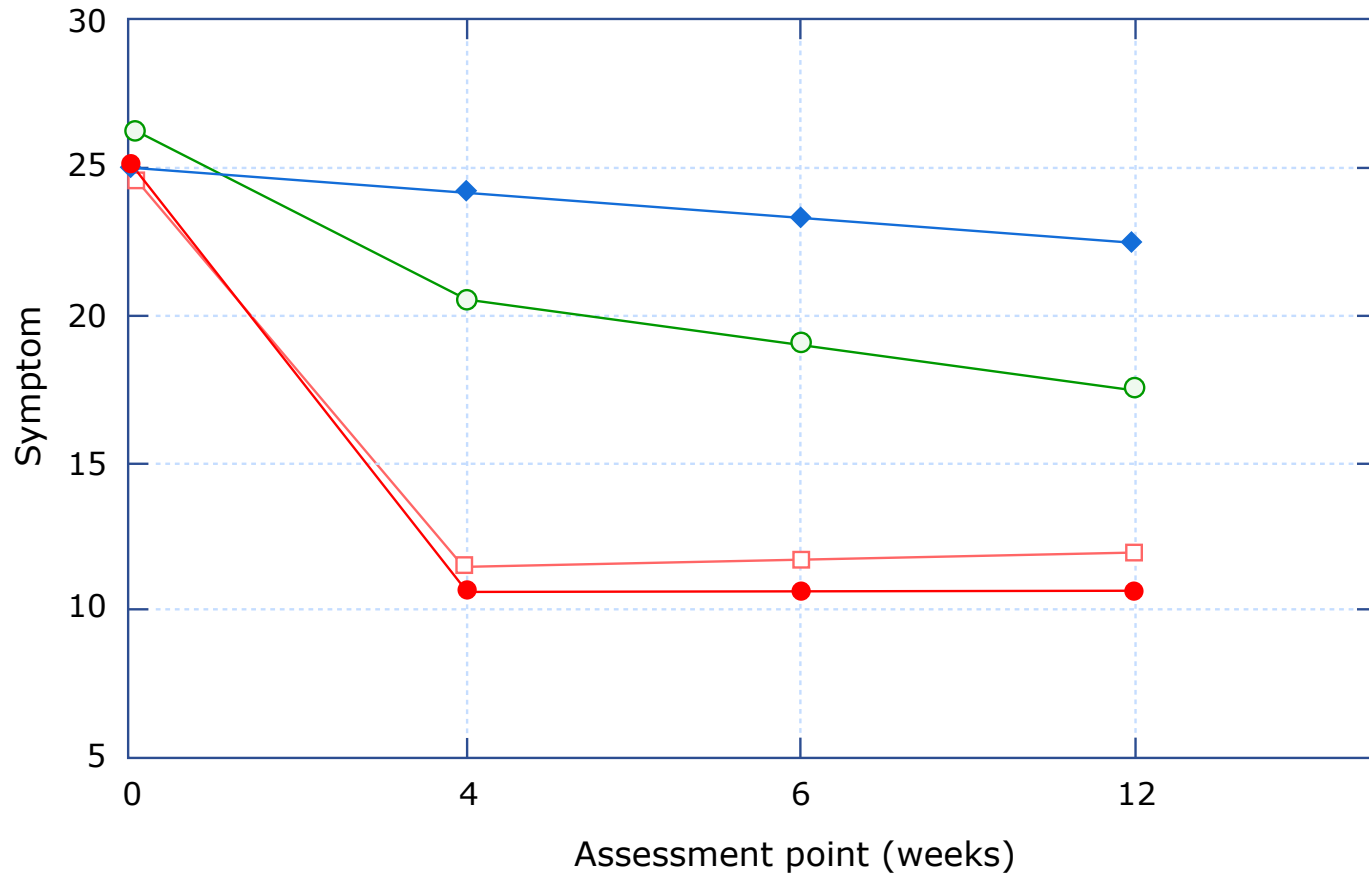
Obsessive Compulsive Disorder (OCD)

- anxiety disorder
- *obsessions* - recurrent, unwanted thoughts
- *compulsions* - repetitive behaviors
handwashing, counting, checking,
cleaning

<http://www.youtube.com/watch?v=Rn1OYIYzgm8>

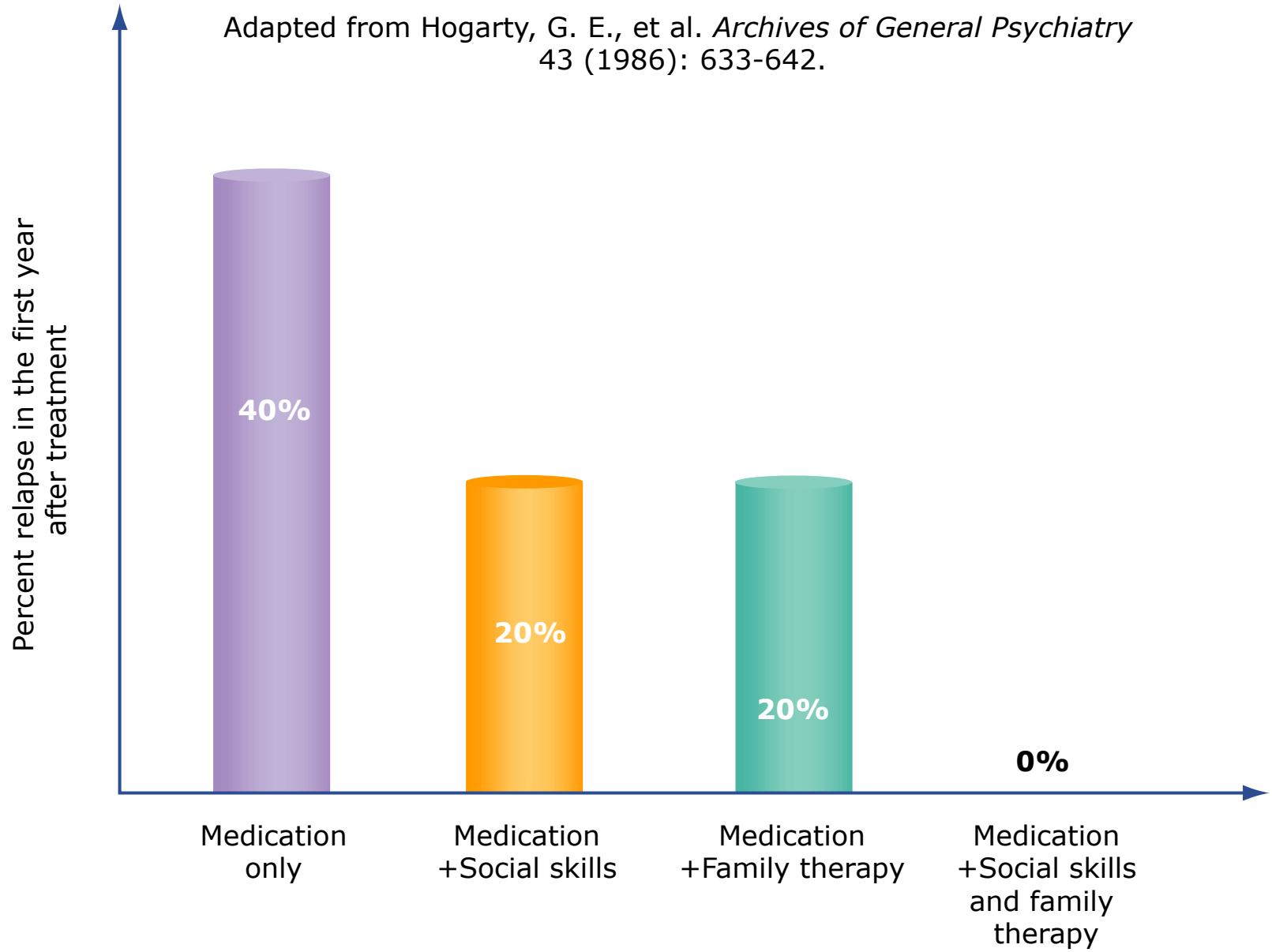
OCD Treatment Study Results

Data from Foa, E. B. et al. *Am J Psychiatry* 162, no. 1 (2005): 151-161.

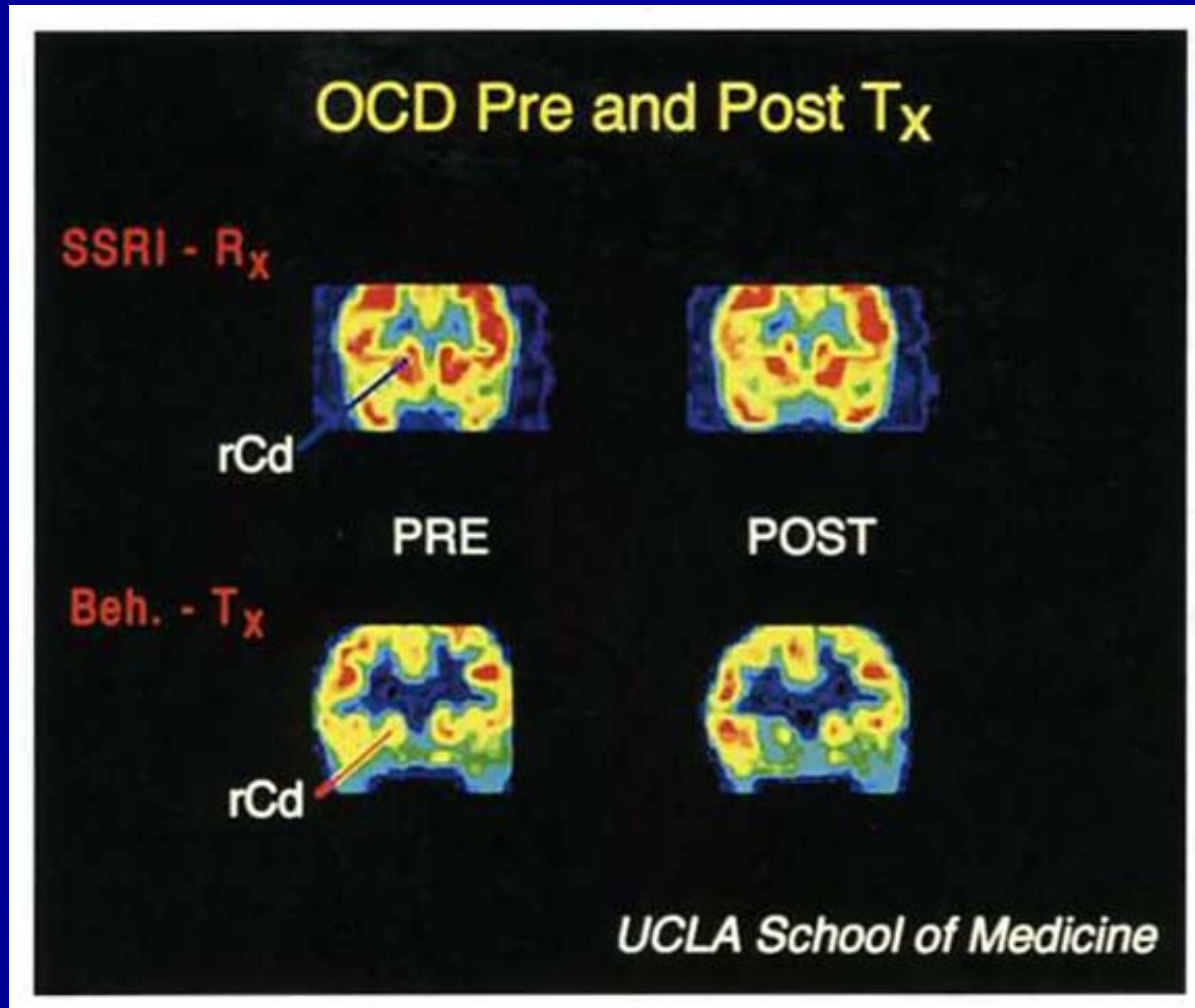


Effectiveness of Antipsychotic Medications and Therapy

Adapted from Hogarty, G. E., et al. *Archives of General Psychiatry* 43 (1986): 633-642.

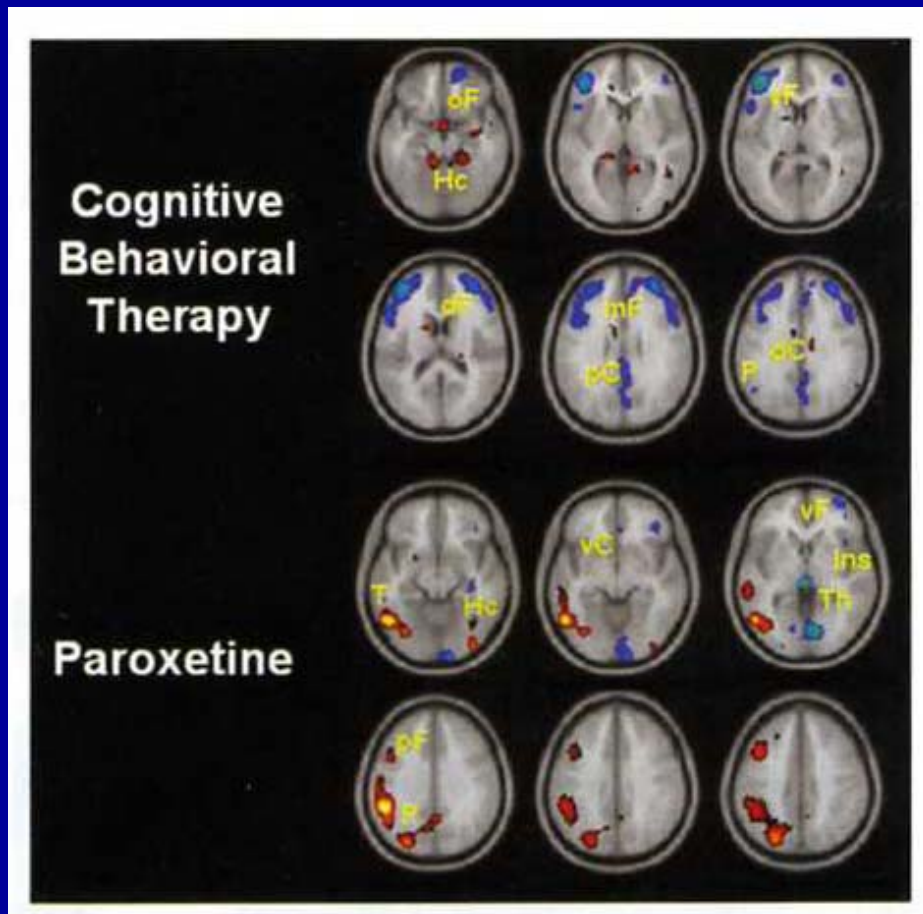


PET Scans of OCD Patients



Basal ganglia shows similar changes with psychotherapy and drug therapy.

Depression: Brain Activity after CBT and Medication Treatments



Different therapies produce different brain activity results. (Orange = increased activity; blue = decreased activity)

DEPRESSION

- fearful, gloomy, helpless, hopeless
- Hamlet "How weary, stale, flat, and unprofitable seem to me all the uses of this world"
- Typical episode is 4-12 months (if untreated) - pervasive dysphoria - intense mental pain, anhedonia (inability to feel pleasure), generalized loss of interest
- 5% of world's population - 8 million in U.S.
- average age of onset is 30, but wide spread - often unnoticed in young - rare to have first episode after 60
- women 2 or 3 times the rate of men
- about 70% who have an episode will have another

DEPRESSION

- **diagnosis requires also at least 3 of the following for a period**
 - **disturbed sleep**
 - **diminished appetite**
 - **loss of energy**
 - **decreased sex drive, restlessness**
 - **slow thoughts/actions**
 - **poor concentration, indecisiveness**
 - **feelings of worthlessness**
 - **guilt**
 - **pessimism**
 - **fixation on death or suicide**
- **Genetic predisposition: Monozygotic twin concordance = 50%; dizygotic = 10% (same as siblings); Environmental - since 1940, a nearly 10-₂₄ year drop in average age of first incidence**

Video clips played in class from
Depression: Beyond the Darkness. Narrated by Hugh
Downs. ABC-TV, episode of *20/20*, airdate August 31,
1990. VHS. MPI Home Video, 1990.

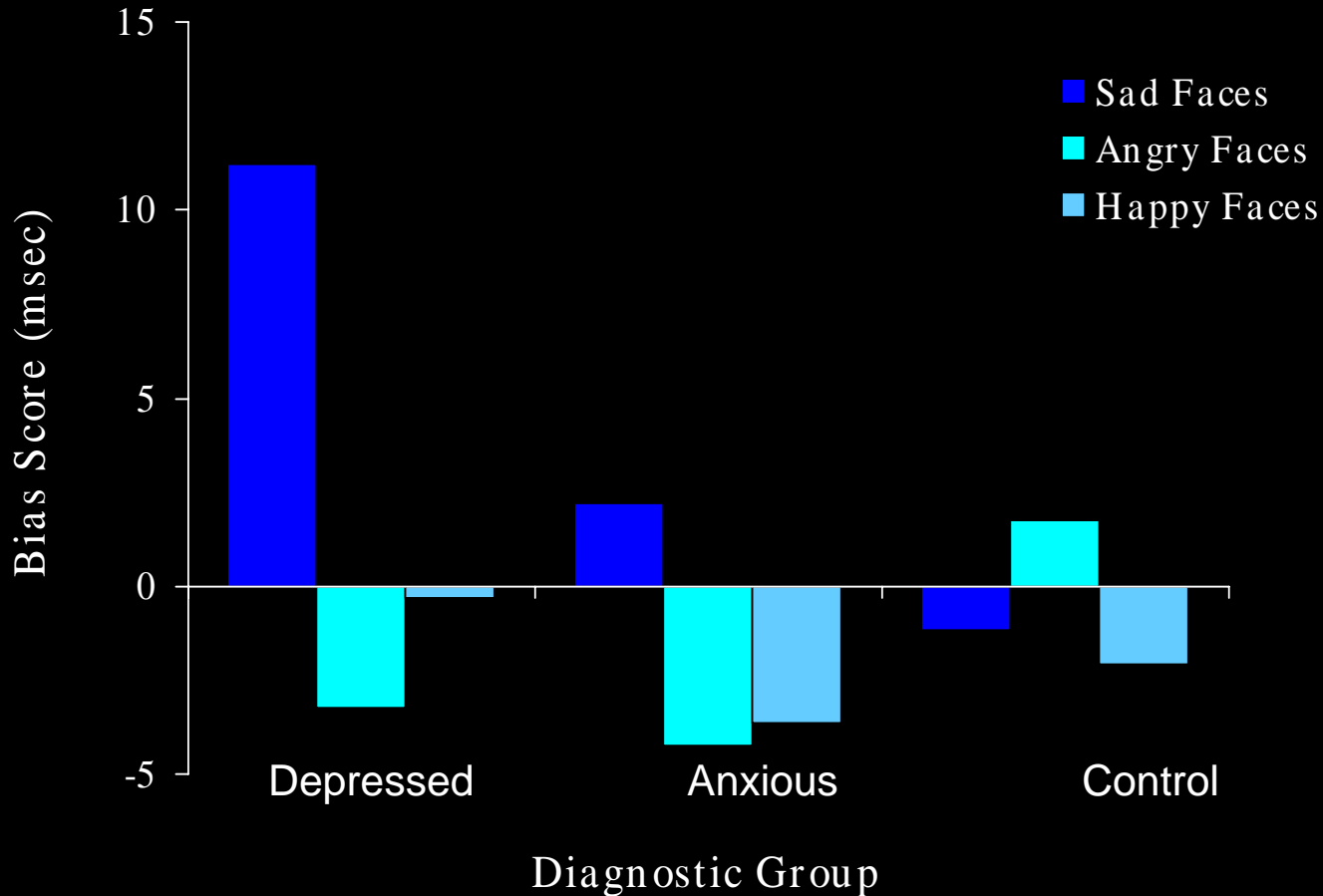
DEPRESSION

- **dot probe task of attentional allocation**
 - **biased attention to sadness in depression**
 - **risk for depression or consequence of depression?**



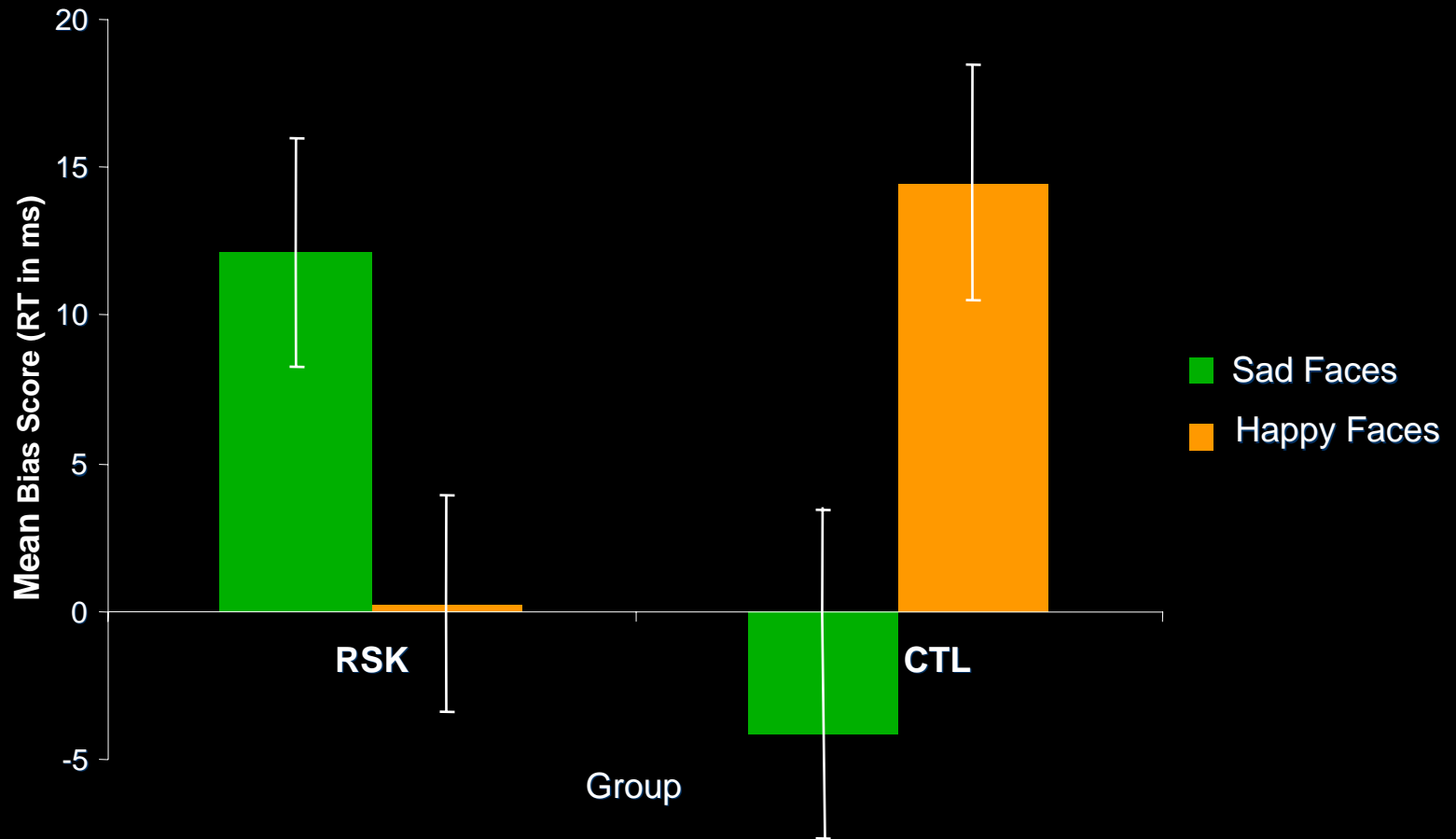


Attentional Biases for Sad, Angry, and Happy Faces



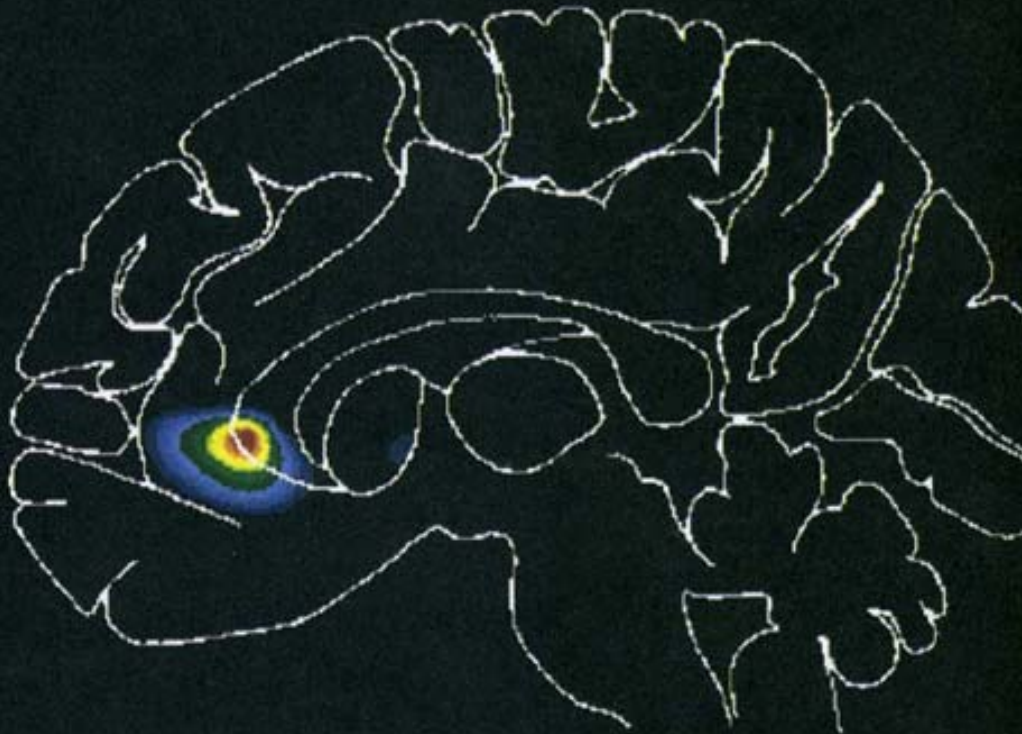
Courtesy of Ian Gotlib. Used with permission.

Attentional Biases for Sad and Happy Faces in High-Risk and Low-Risk Girls



Courtesy of Ian Gotlib. Used with permission.

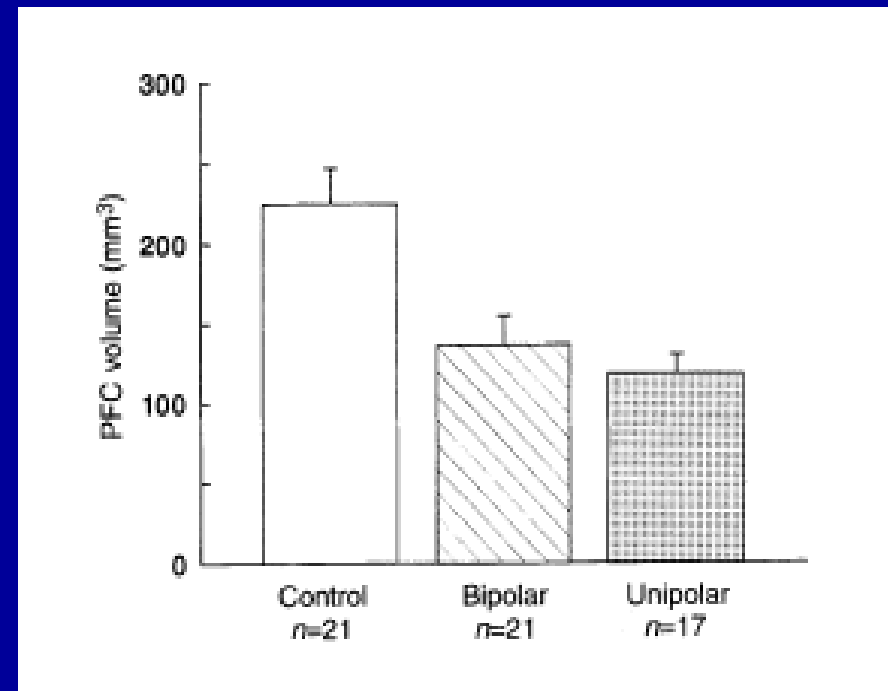
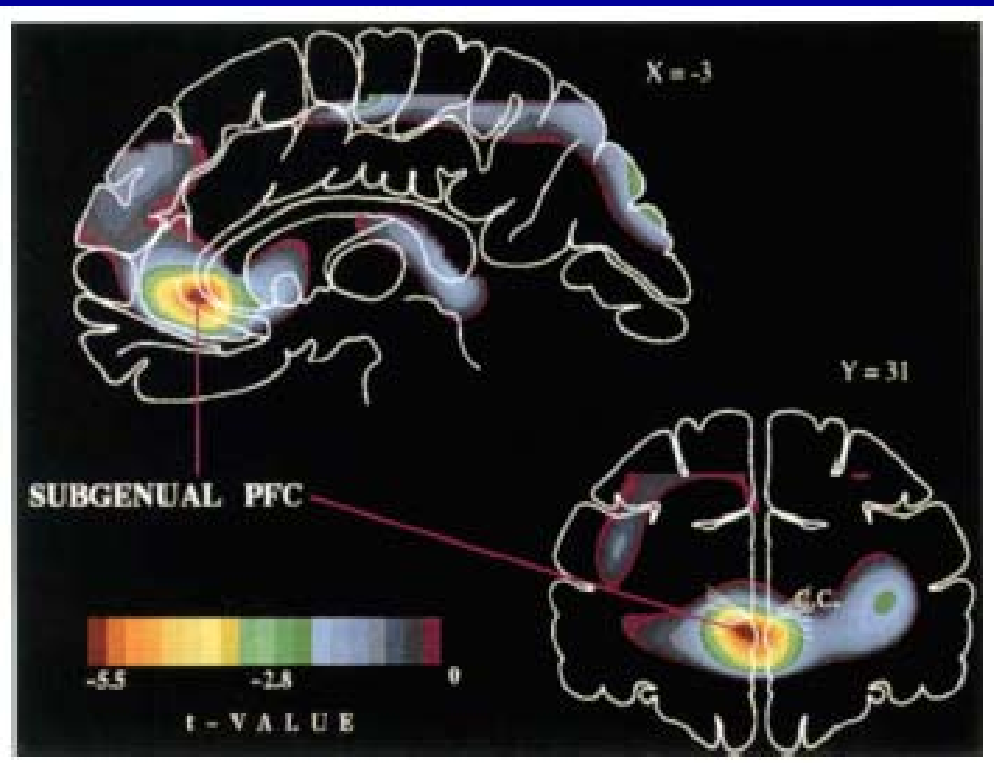
DEPRESSION & SUBGENUAL ANTERIOR CINGULATE



This PET scan was also produced by subtracting scans of normal subjects from scans of depression patients. It reveals a tiny area buried deep along the midline in the frontal lobe (also known as the orbitofrontal cortex because of its position just above and behind the eyes) which may play a key role in the symptoms of depression. Here it exhibits reduced metabolism in patients with depression.

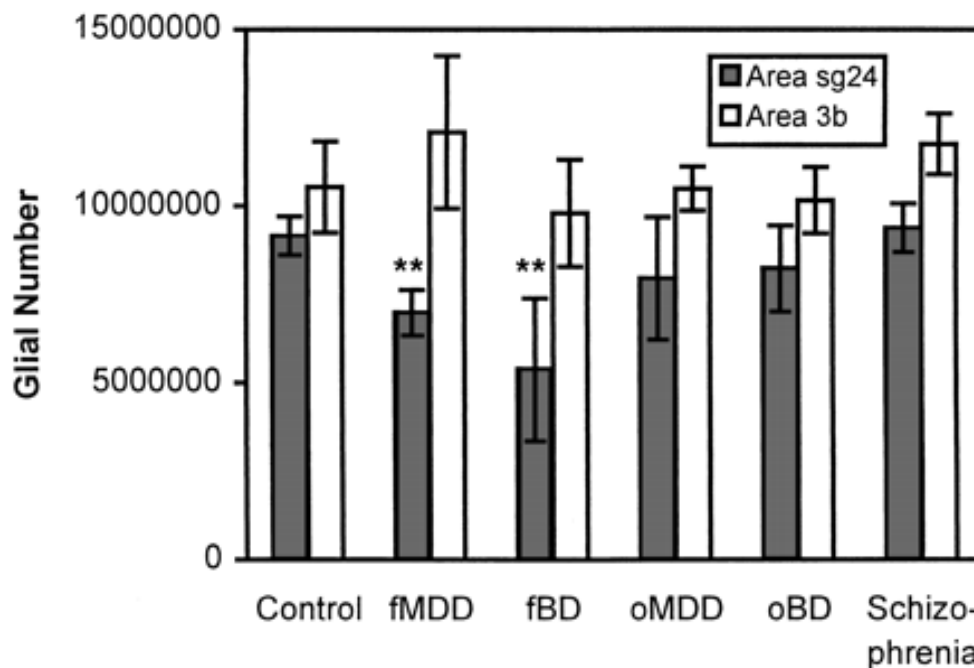
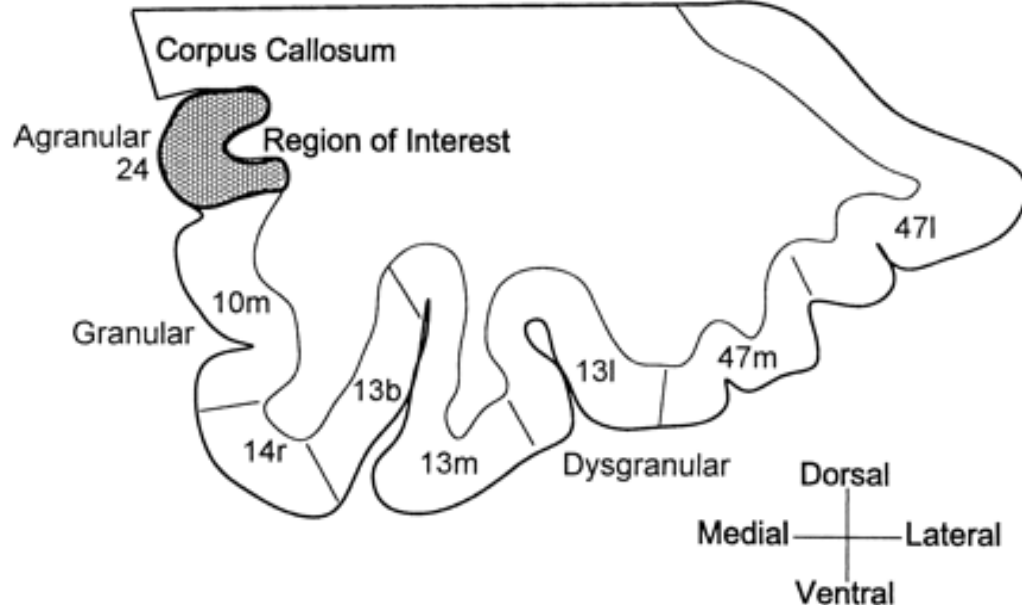
Courtesy of Wayne Drevets. Used with permission.

REDUCED BRAIN VOLUME IN DEPRESSION IN SUBGENUAL ANTERIOR CINGULATE

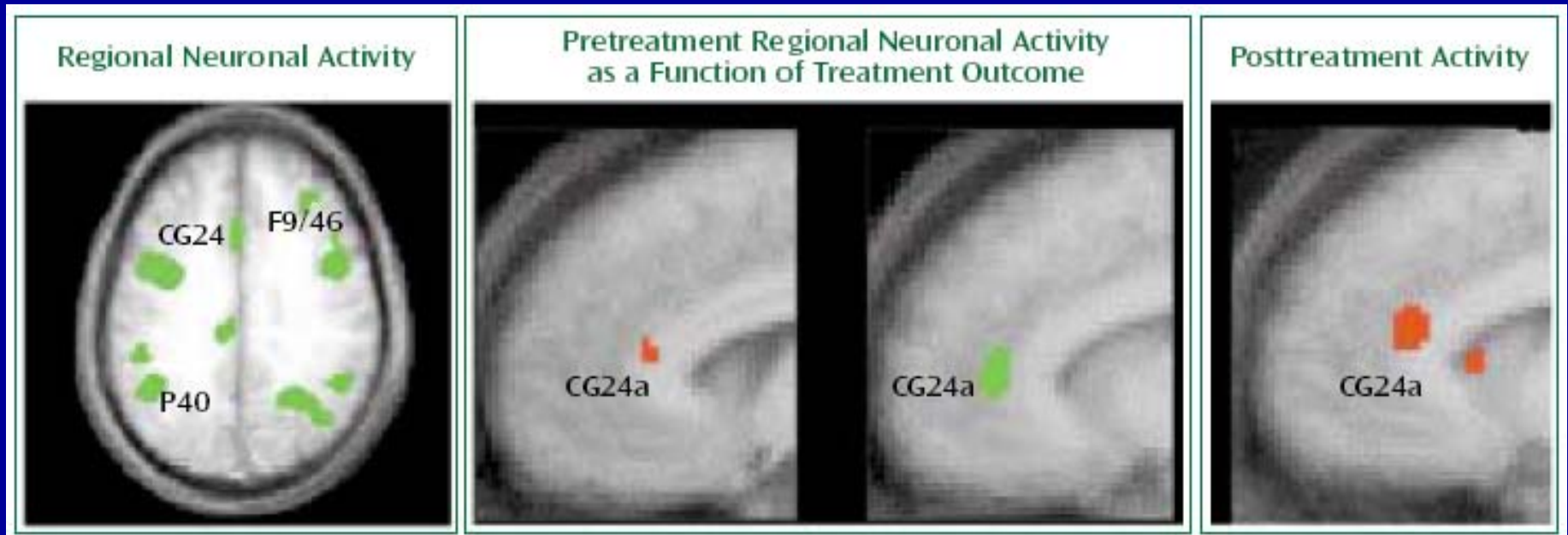


Reprinted by permission from Macmillan Publishers Ltd: Nature. Source: Drevets, W. C., et al. "Subgenual Prefrontal Cortex Abnormalities in Mood Disorders." *Nature* 386 (1997): 824-7. © 1997.

**REDUCED
NUMBER OF
GLIAL CELLS
IN
SUBGENUAL
ANTERIOR
CINGULATE
CORTEX
IN
DEPRESSION
(no change in
neurons)**



RELATION OF ACTIVATION IN SUBGENUAL ANTERIOR CINGULATE CORTEX TO DRUG TREATMENT OUTCOME



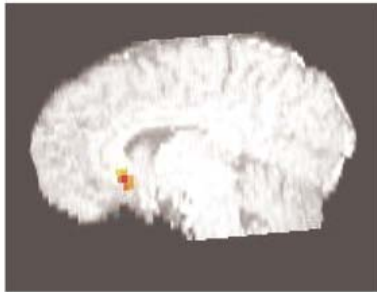
**BETTER
OUTCOME**

**WORSE
OUTCOME**

**AFTER
TREATMENT**

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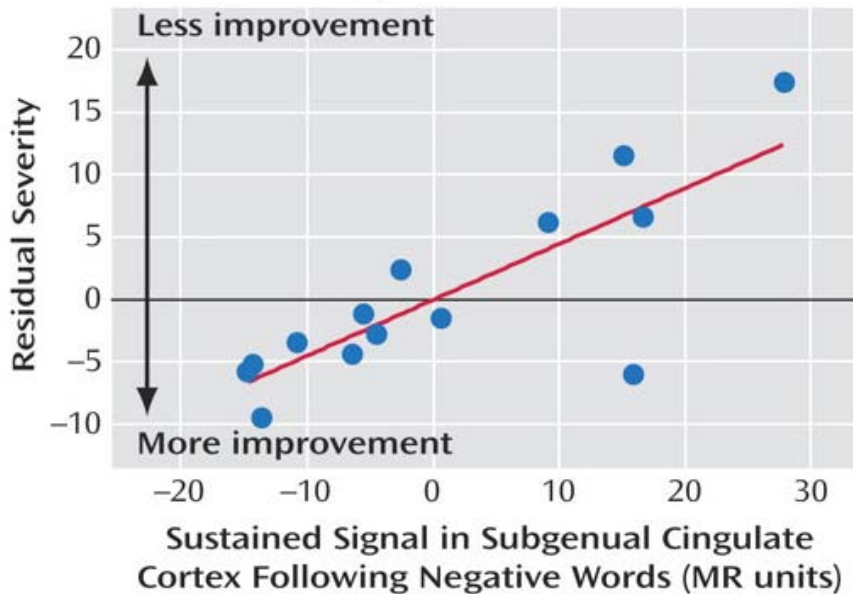
A. Region Examined



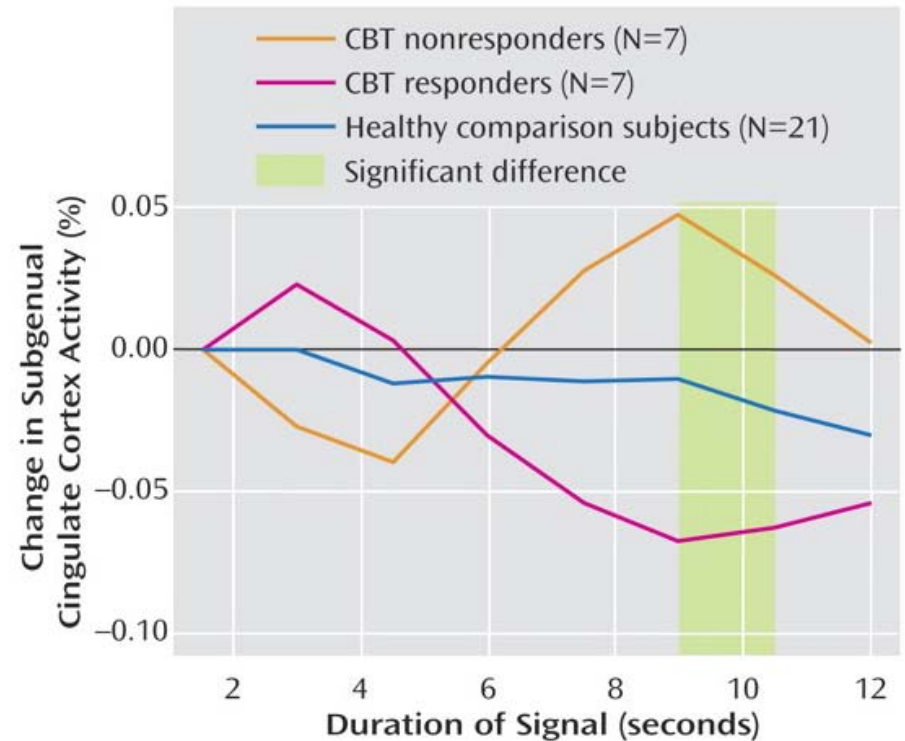
Subgenual Cingulate Cortex

PREDICTING CBT OUTCOME IN DEPRESSION

B. Relationship Between Regional Reactivity to Negative Words and Residual Depressive Severity Following Treatment With Cognitive Behavior Therapy



C. Regional Reactivity to Negative Words in Patients With Unipolar Depression, by CBT Response Status, Relative to Healthy Comparison Subjects



Treatment for Depression

- **medications (27 million people in US 2005, \$9.6 billion in 2008 sales)**
- **CBT**

Current Treatment for Depression is Suboptimal

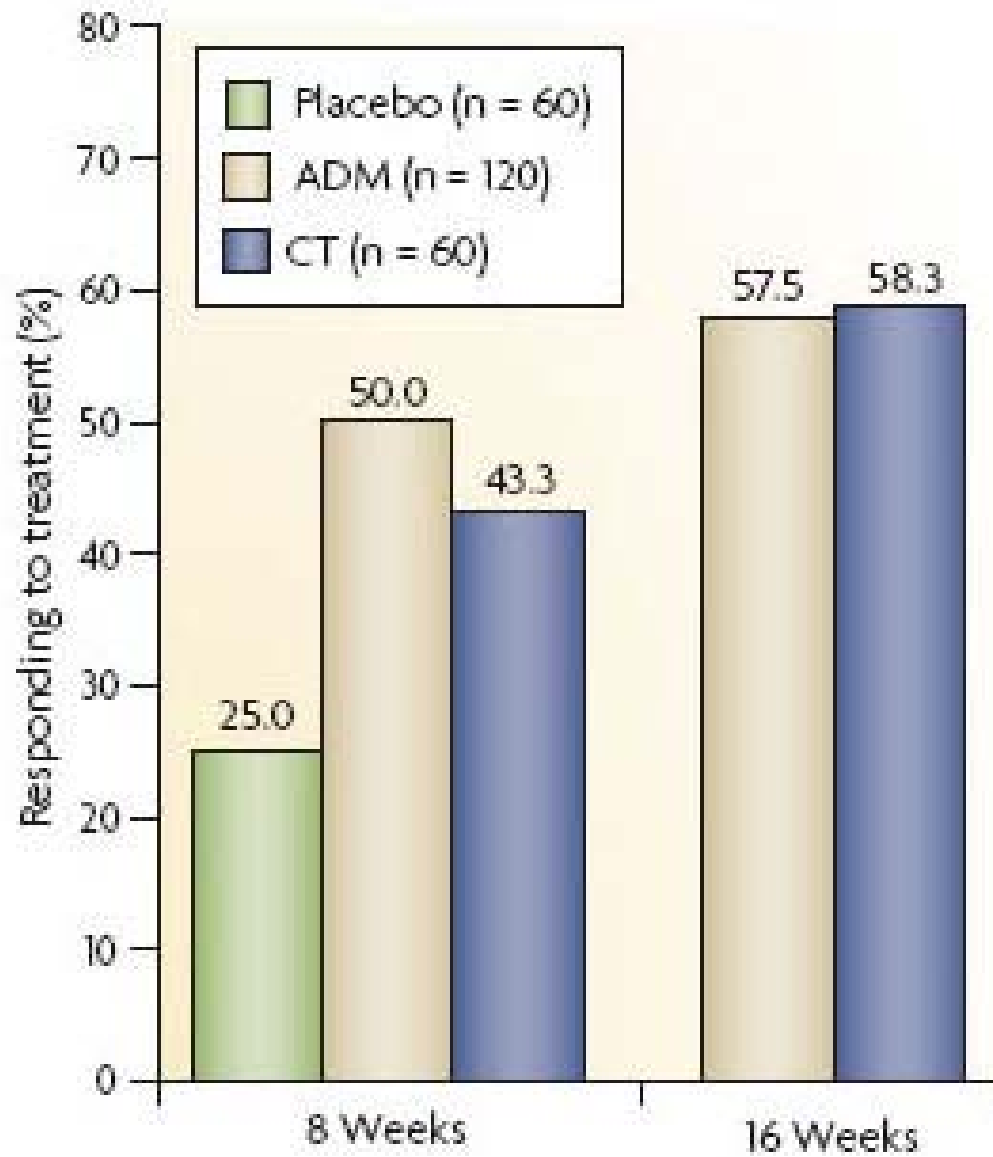
- **Only partially effective**

As many as $\frac{1}{2}$ of patients do not achieve remission (Petersen et al., 2005)

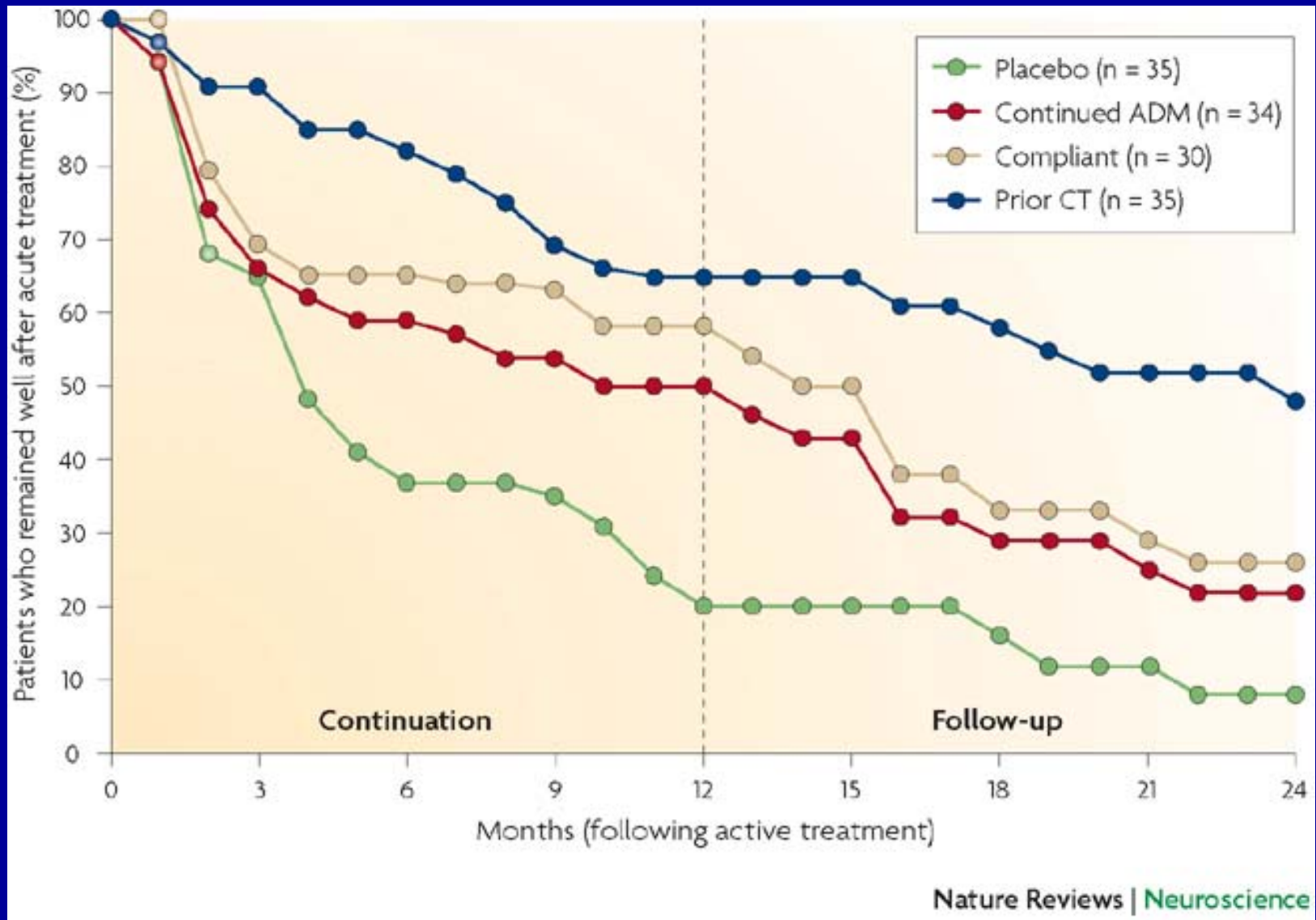
Residual symptoms are common among patients achieving remission (Nierenberg, 1999)

- **Trial and Error**

Selecting correct treatment takes months, causing attrition



Nature Reviews | Neuroscience



Reprinted by permission from Macmillan Publishers Ltd: Nature Reviews Neuroscience. Source: DeRubeis, R. J., et al. "Cognitive Therapy Versus Medication for Depression: Treatment Outcomes and Neural Mechanisms." *Nature Reviews Neuroscience* 9 (2008): 788-96. © 2008.

Treatment for Depression

- clinical trials

drug – random assignment, double-blind with placebo

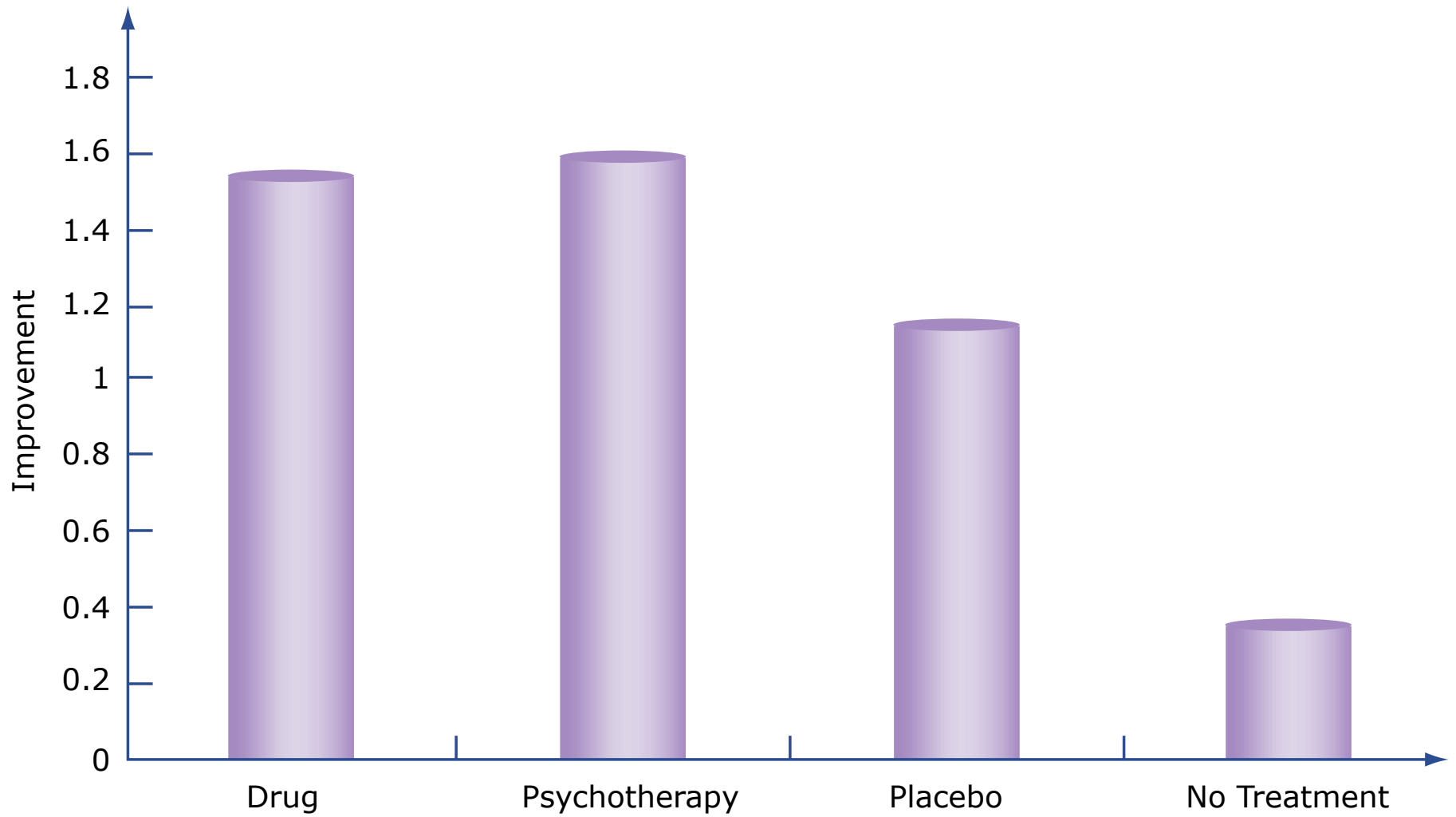
outcome – response vs. remission

interviews – physician – Hamilton Depression Rating Scale

strong placebo response

regression to the mean from study entry?

real response to placebo?



Treatment for Depression

recent meta-analyses

- **Kirsch** – no effect of drug (above placebo, about 75% of effect) – apparent difference is due to patients realizing they are on active drug from side effects – greater side effects associated with better drug response (80% of patients guess correctly they are on drug) – no drug/placebo difference if placebo causes side effects
- **Fournier** – little or no drug benefit above placebo for mild-to-moderate or severe depression; benefit for patients with very severe depression

ATTENTION DEFICIT DISORDER (ADHD/ADD)

- **INATTENTION**
- **HYPERACTIVITY (80%)**
- **IMPULSIVITY**
- **DIAGNOSIS by exclusion**
- **PREVALENCE 2 million in US**
tripled since 1981
increased 2.5 times since 1990

How Do Clinicians Make The Diagnosis?

- History from parents and physical exam
- Collection of data from school and parents using questionnaires

Prevalence of ADHD

- Ranges from 1.7 to 16.1% in various studies
- Different diagnostic methods have been used to establish the prevalence
- Different DSM manuals - DSM III, DSM IIIR, and now DSM IV
- Different settings - by country, by profession
- Wolraich – same German population, incidence changed from 6 to 12% DSM 3R to DSM 4

Attention Deficit Hyperactivity Disorder (ADHD)

- **PREVALENCE:** 3 - 5% of school-age children
- **Impairs social and academic adjustment in childhood**
 - predicts antisocial behavior, substance abuse and adverse occupational and social adjustment in adulthood
- **TREATMENT:** Stimulants, e.g. methylphenidate (Ritalin)
- **ETIOLOGY:** genetic
 - rates among relatives of probands - 7 times
 - twin studies - .76 heritability
 - candidate genes - dopaminergic

DIAGNOSTIC CRITERIA

- **INATTENTION** (> 6 for at least 6 months to a degree that is maladaptive and age-inappropriate)
 - careless mistakes in schoolwork or other activities
 - difficulty sustaining attention in tasks or play
 - does not seem to listen when spoken to directly
 - does not follow instructions or finish tasks
 - difficulty organizing tasks and activities
 - avoids tasks engaging sustained mental effort
 - loses things
 - easily distracted by extraneous stimuli
 - forgetful in daily activities

- **HYPERACTIVITY-IMPULSIVITY** (> 6 for at least 6 months to a degree that is maladaptive and age-inappropriate)

Hyperactivity

- fidgets or squirms in seat
- leaves seat in classroom
- runs about or climbs excessively
- difficulty playing quietly
- is “on the go” or acts as if “driven by a motor”
- talks excessively

Impulsivity

- blurts out answers before questions are completed
- difficulty awaiting turn
- interrupts or intrudes on others’ conversations or games

- **Symptoms present before age 7 years**
- **Symptoms present in 2 or more settings (home/school)**
- **Diagnosis by exclusion of following:**
 - **pervasive developmental disorder**
 - **sensory deficits**
 - **allergies**
 - **psychiatric conditions that “mimic” ADHD**
e.g., depression
- **Subtypes -**
 - **Combined-type - both inattention and hyperactivity-impulsivity**
 - **Inattention-type - inattention only**
 - **Hyperactive-impulsive - hyperactivity-impulsivity only**

Long-term consequences

If untreated -> secondary problems:

- depression
- anxiety
- substance abuse
- academic failure
- work problems
- family problems
- emotional distress

Multimodal Treatment Study of Children with Attention Deficit Hyperactivity Disorder (MTA)

579 children – 14 month study

- (1) medication management alone;**
- (2) behavioral treatment alone;**
- (3) a combination of both; or**
- (4) routine community care**

MTA Study

- (1) medication management alone;
monthly 30 min physician - titration -
child/parent**
- (2) behavioral treatment alone;
35 visits; 8-week summer camp**
- (3) a combination of both; or**
- (4) routine community care
1-2 times/year**

MTA Study

Best Outcomes

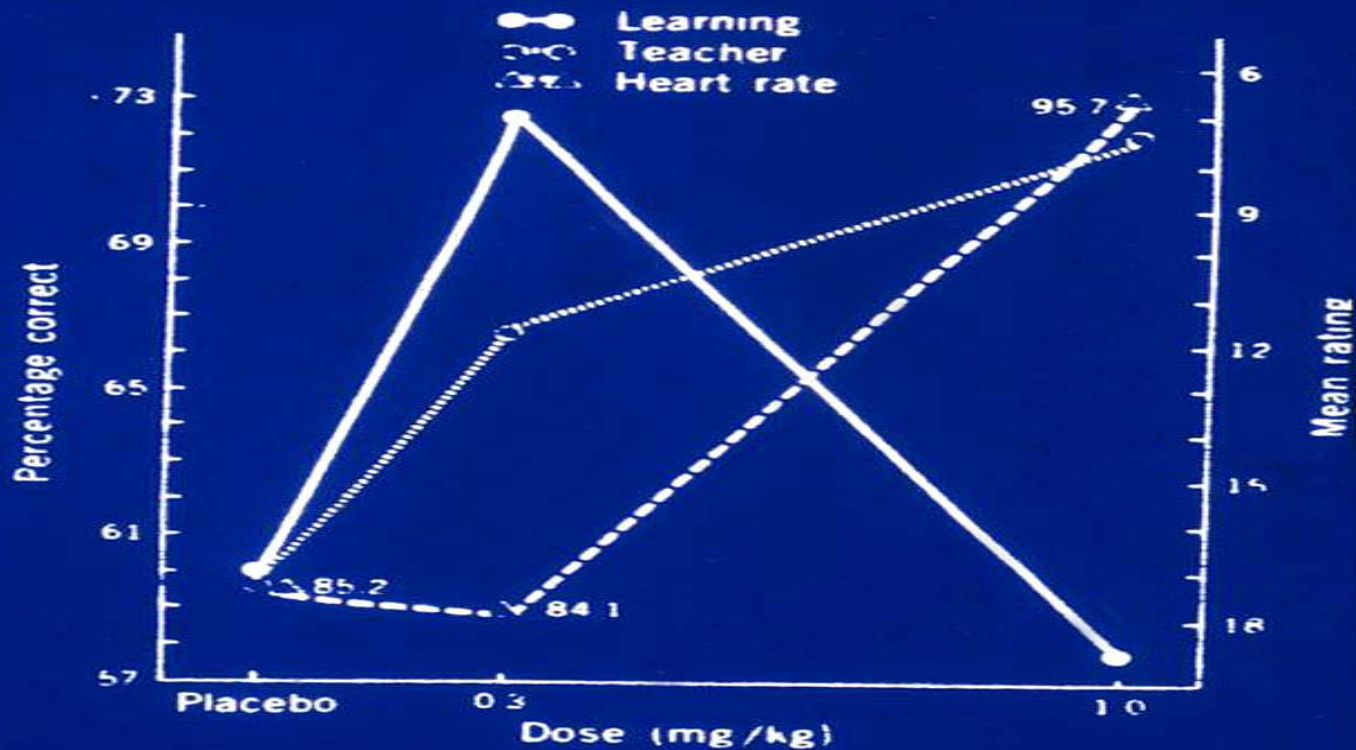
medication management alone or a combination of both

some gains for combined on anxiety, academic performance, oppositionality, parent-child relations, and social skills; lower doses of medications

MTA Study

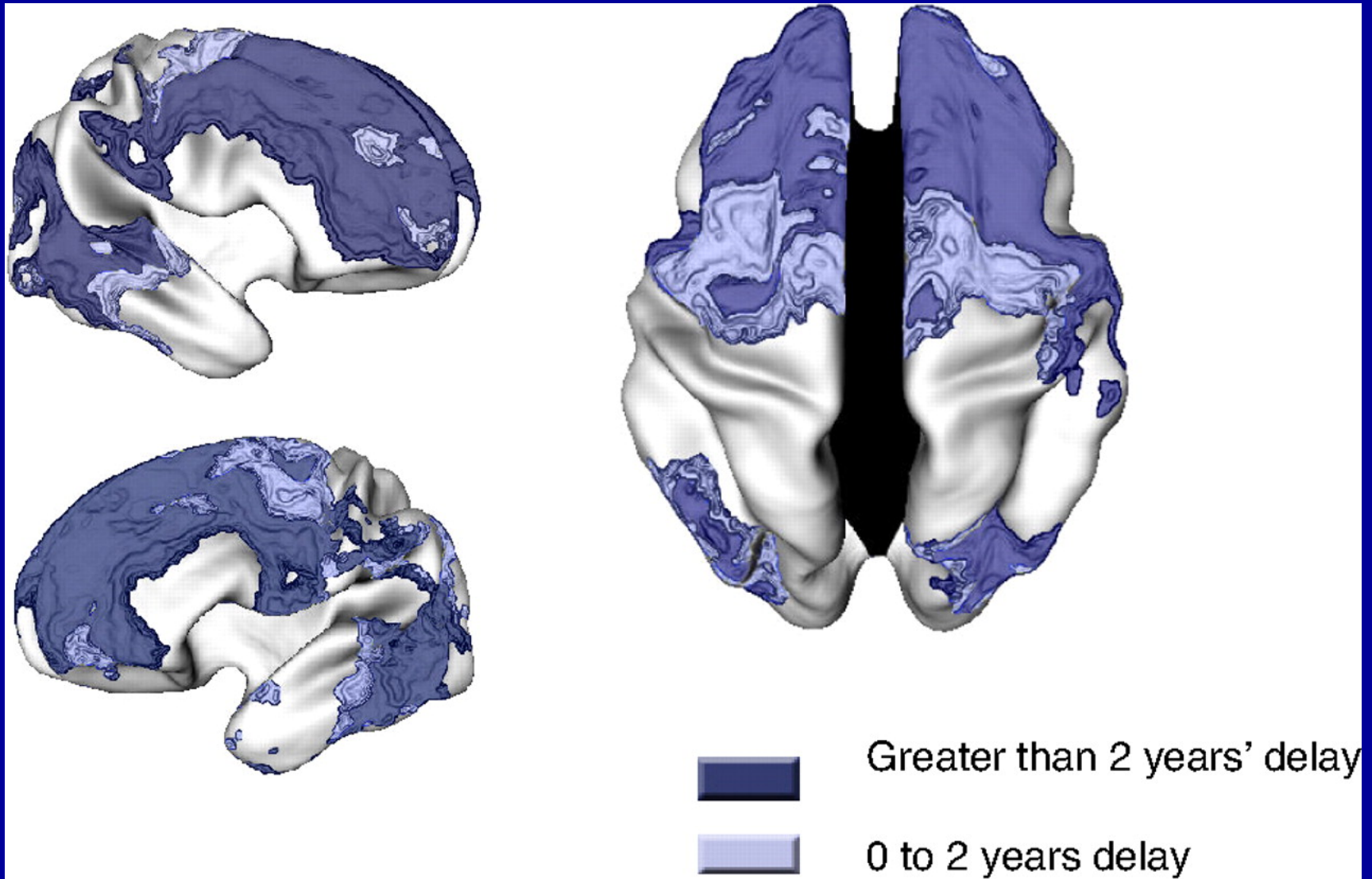
- 8 years later no difference
- 61.5% stopped taking medication
- no difference between those who did or did not stop taking medications

BEST DOSE?



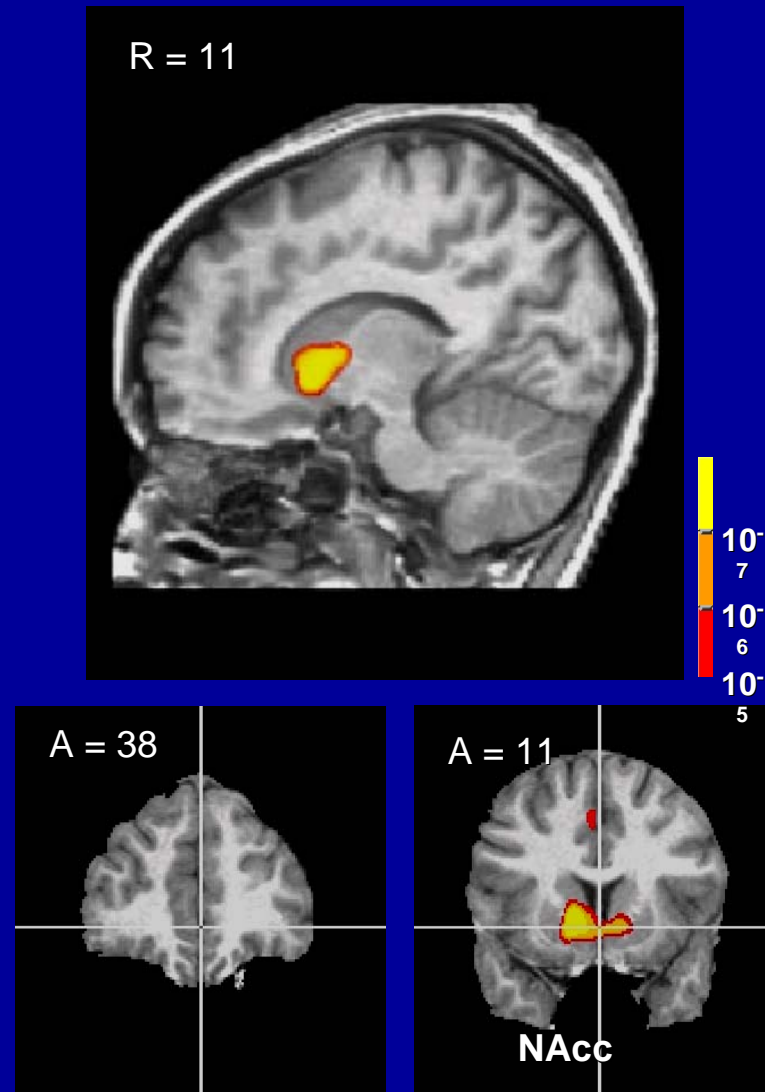
Sprague and Sleator, Science, 1977

Regions where the ADHD group had delayed cortical maturation, as indicated by an older age of attaining peak



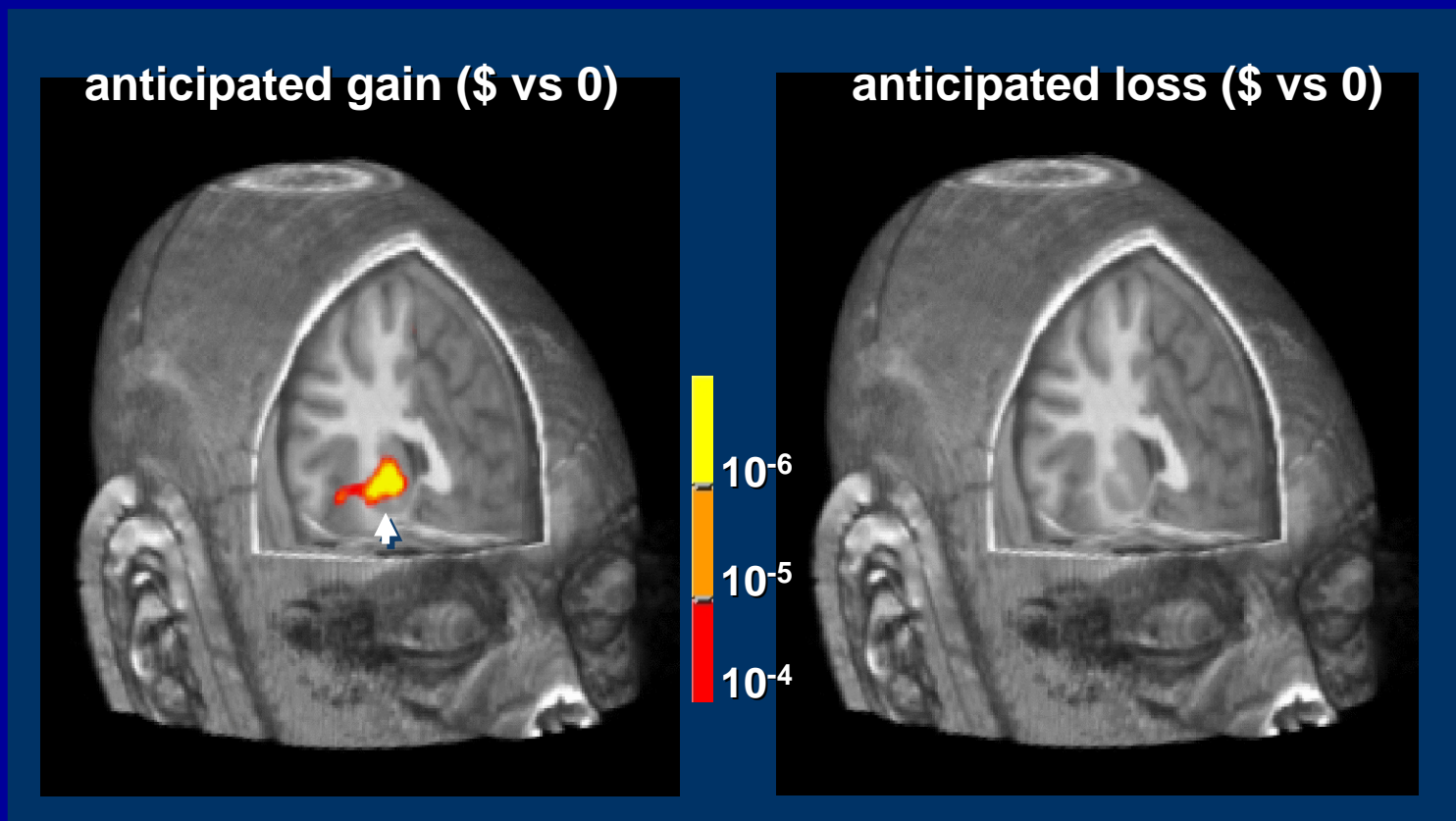
Courtesy of National Academy of Sciences, U.S.A. Used with permission. Source: Shaw, P., et al. "Attention-Deficit/Hyperactivity Disorder is Characterized by a Delay in Cortical Maturation." *PNAS* 104, no. 49 (2007): 19649-54. Copyright ©2007 National Academy of Sciences, U.S.A.

Nucleus Accumbens recruited by anticipation of responding for a reward versus nonreward



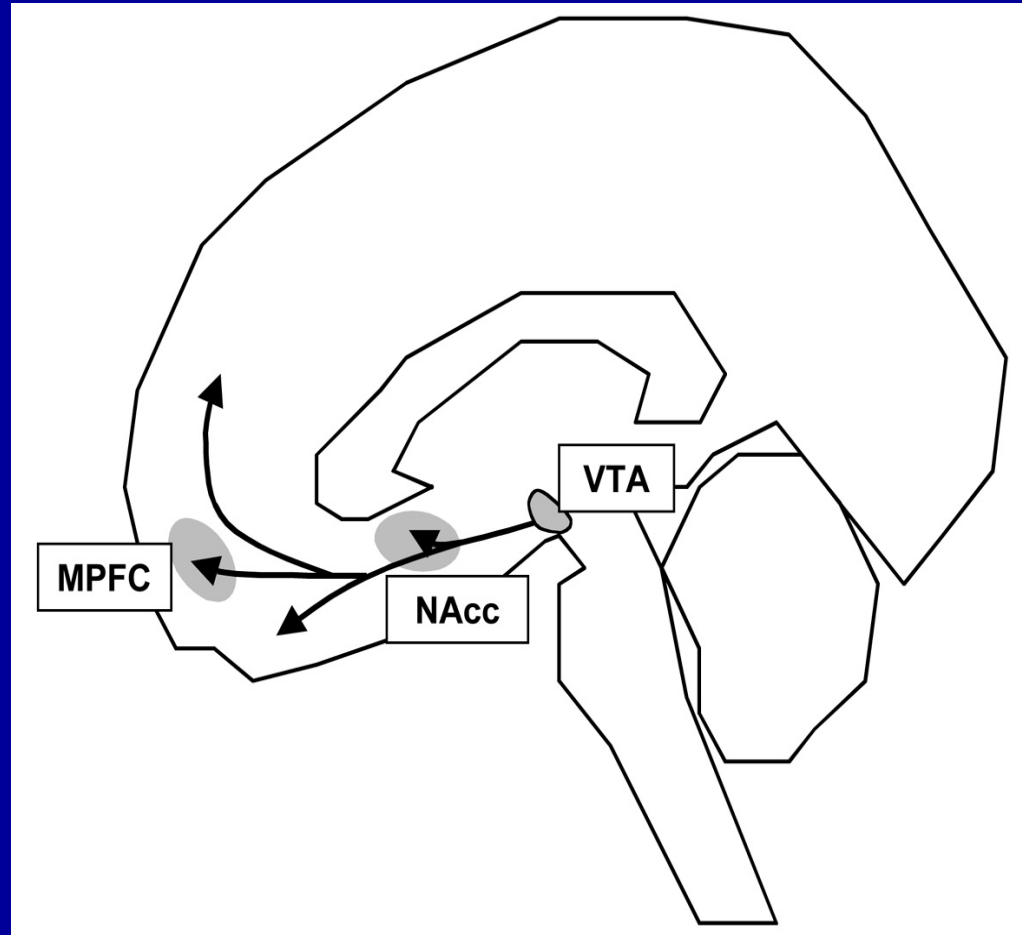
Courtesy of Brian Knutson.
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Gain anticipation activates Nucleus Accumbens



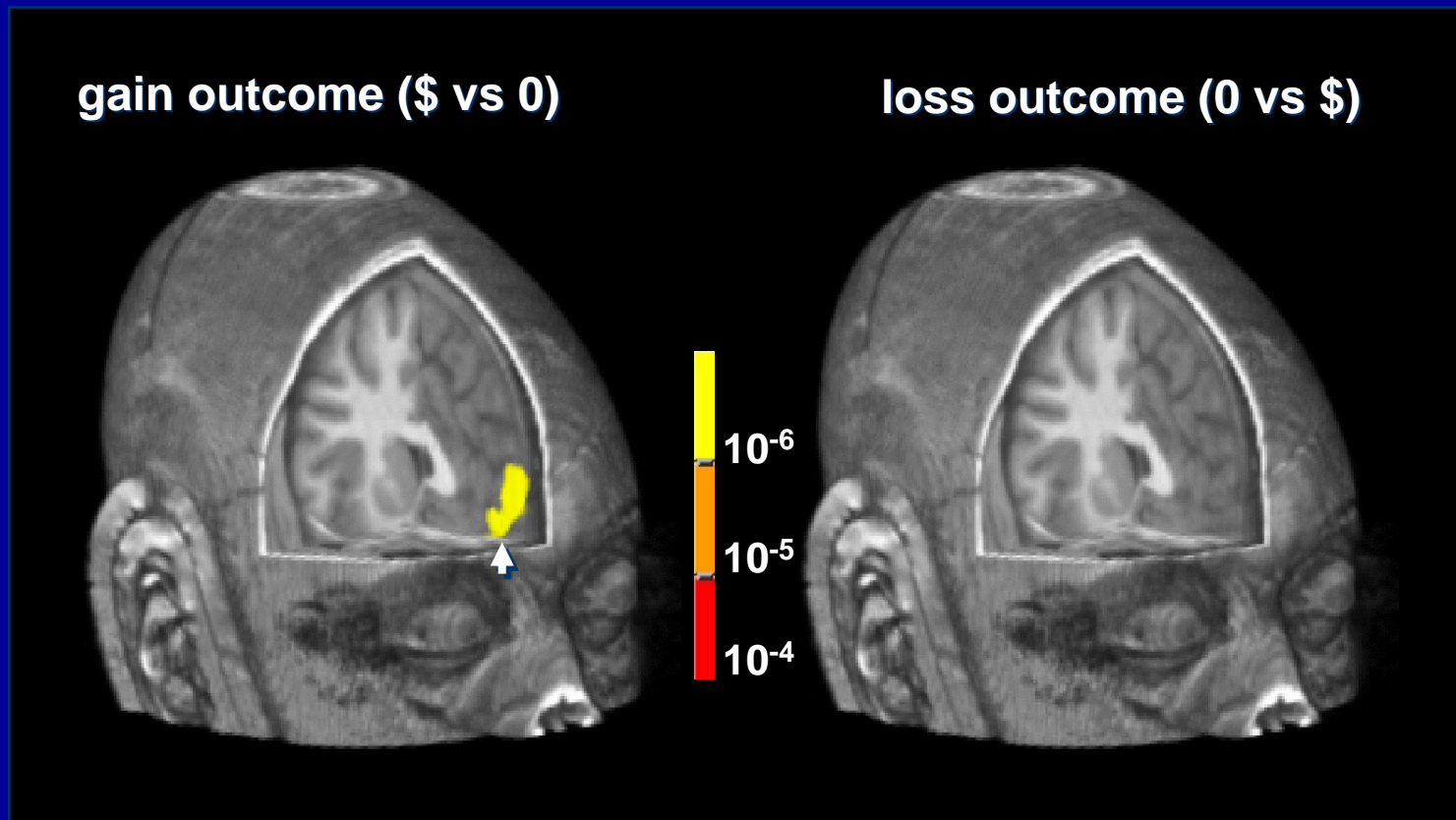
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Mesolimbic Dopamine Projections



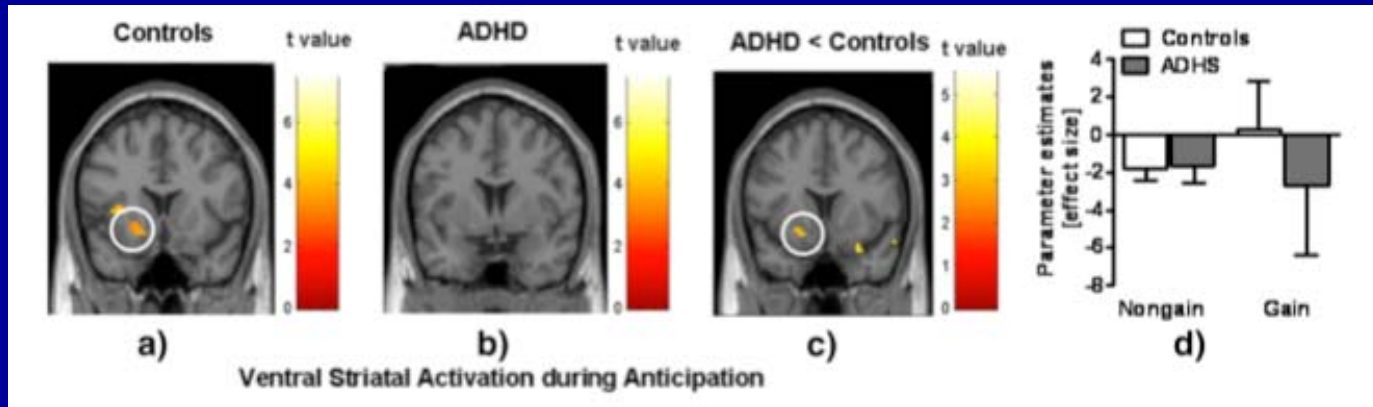
Knutson, B., and S. E. B Gibbs (2007) *Psychopharmacology*

Gain outcomes activate MPFC

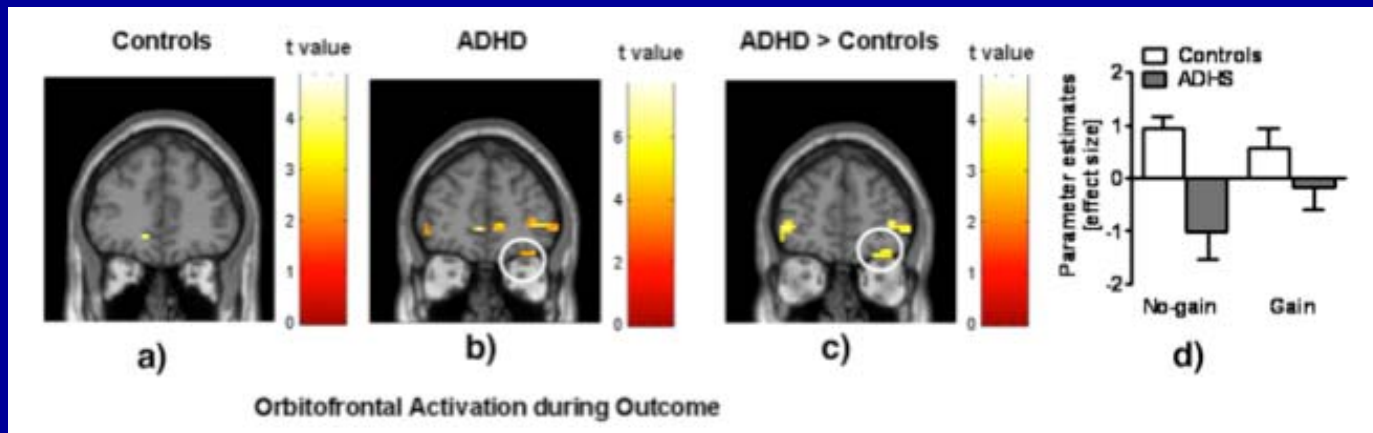


Courtesy of Brian Knutson. Used with permission

LESS RESPONSE TO REWARD ANTICIPATION IN ADHD

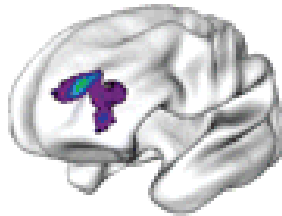


GREATER RESPONSE TO REWARD OUTCOME IN ADHD

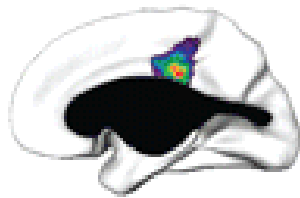


Treatment With Psychostimulants Does Not Slow Development Of Cerebral Cortex

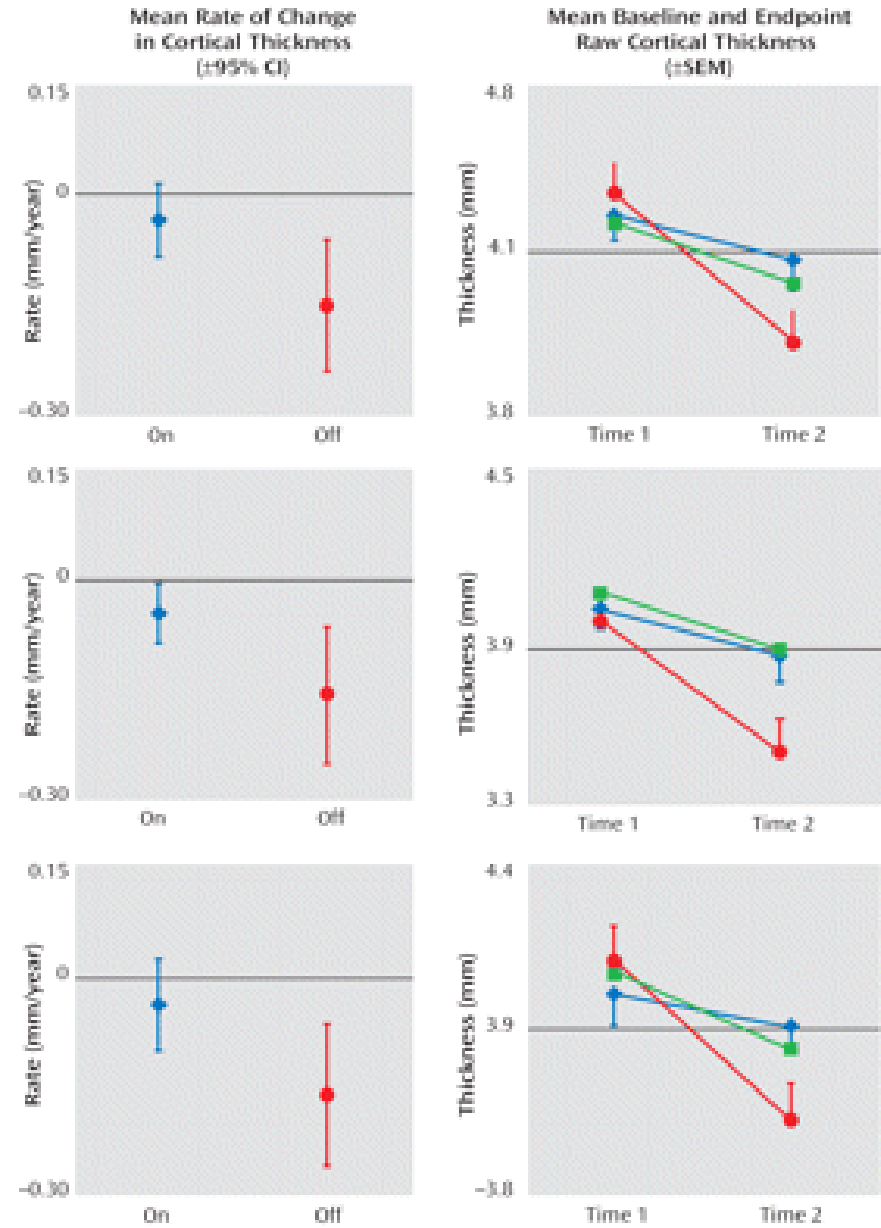
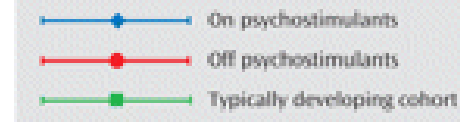
Left middle/inferior frontal gyrus



Right medial prefrontal cortex (motor region)



Right posterior parieto-occipital cortex



Questions

- Does brain function differ in ADHD and control children?

Do brain regions involved in inhibitory control function differently in children with ADHD?

- Does Ritalin have different effects on brain function in ADHD and control children?

- Treatment by stimulants (e.g. Ritalin)
- Brain changes that mediate effectiveness are unknown
- Effects in control children are unknown

Participants

		Age (yrs)	WISC IQ		
			Verb	Perf	Full
ADHD n = 10	Mean	10.5	121	117	120
Control n = 6	Mean	9.3	128	118	124

Go-No-Go Task

Go

25 s

No-Go

25 s

Go

25 s

No-Go

25 s

6 cycles

.....
5 mins

“Respond to
all letters”

“Do not
respond to X”

H

L

P

X

C

X

.5 sec exposure
1.4 sec ISI

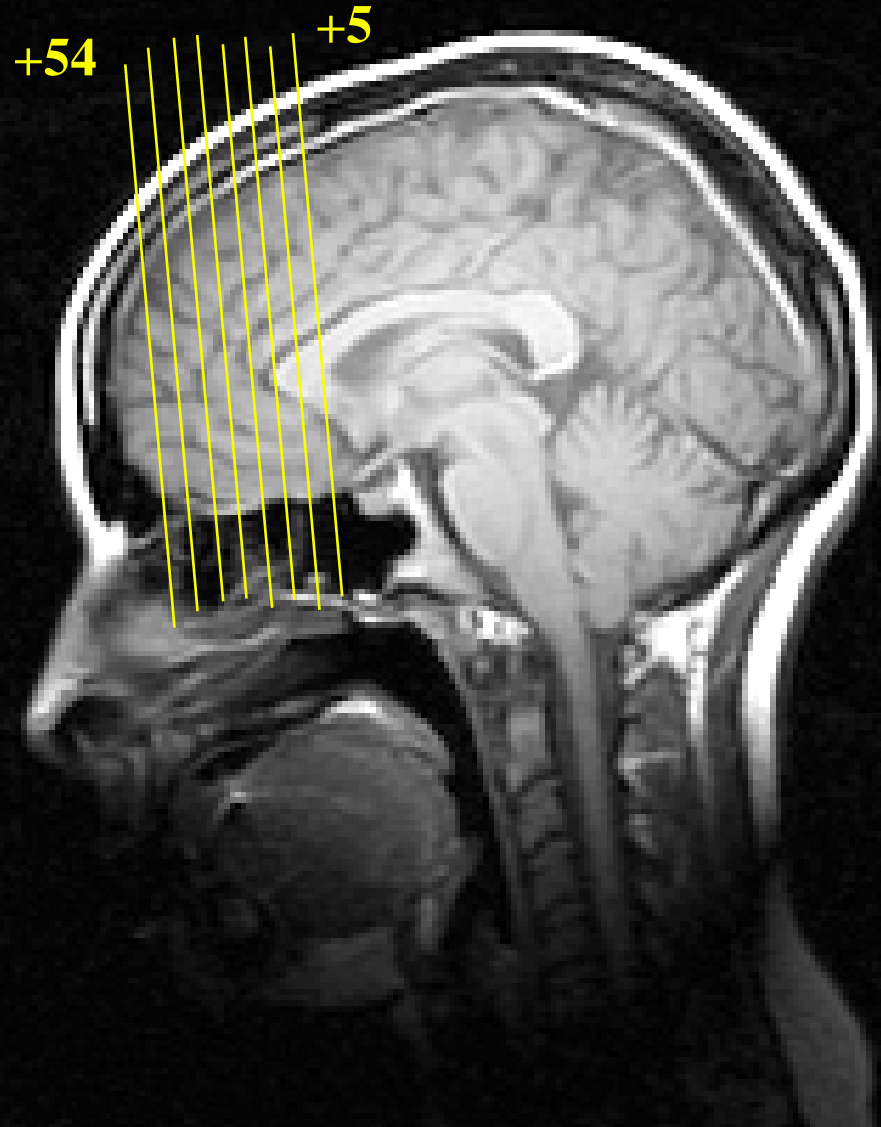
50 %

12

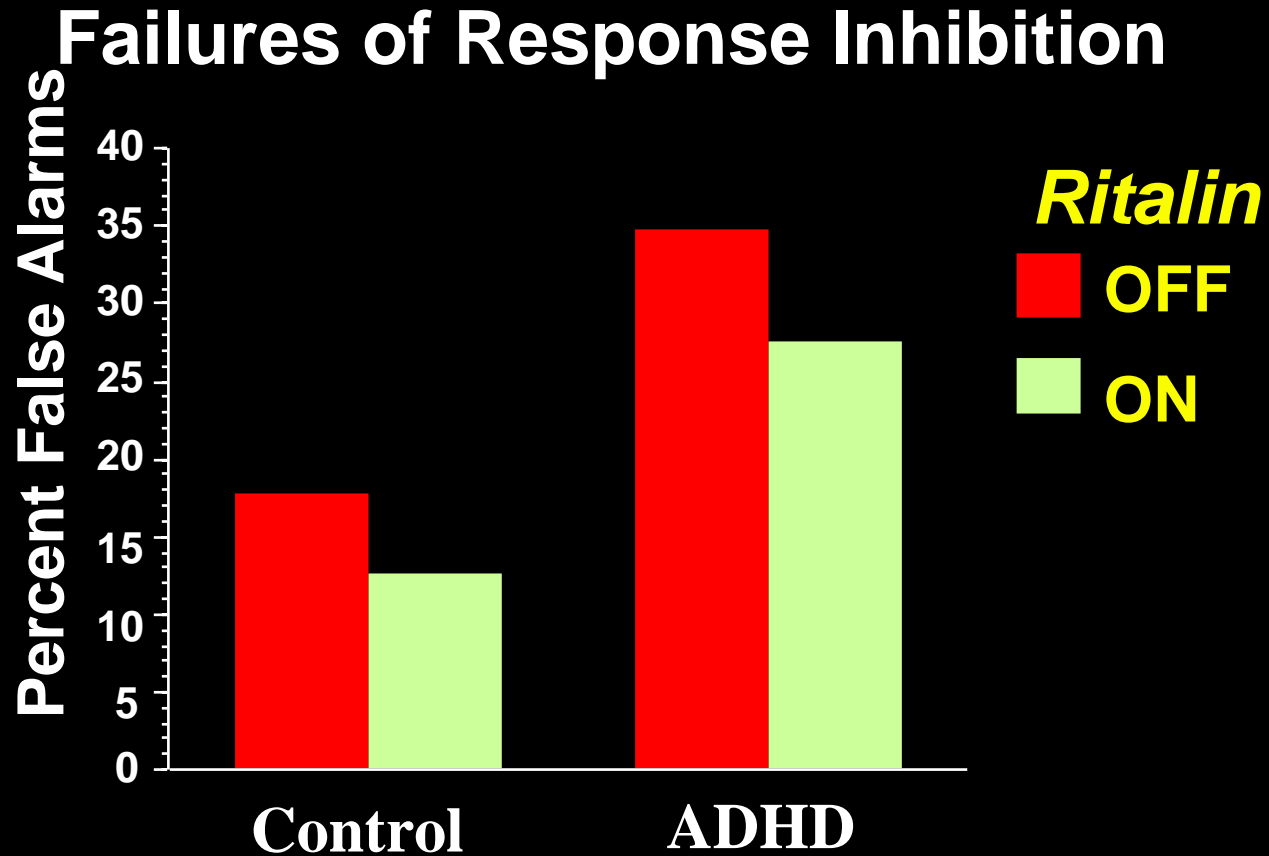
12

Functional Scanning Parameters

- 1.5 T GE
- Gradient Echo Spiral Pulse Sequence
- TR/slice = 90 ms, TE = 40 ms
- Flip angle = 65
- 4 interleaves
- FOV = 36 cm
- 8 coronal slices: 6 mm thick
1 mm inter-slice space
- Continuous acquisition for 300 s
- In-plane resolution: 2.35 mm
- Image acquisition = 2.88 sec
- Bite-bar to minimize motion
- Time-series data analysis:
Friston et al., 1994

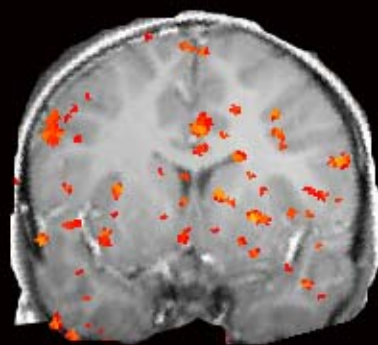


Effect of Ritalin on Performance

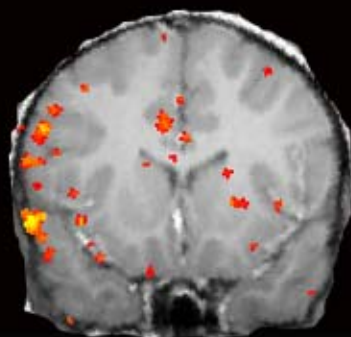


Ritalin improved performance in both groups

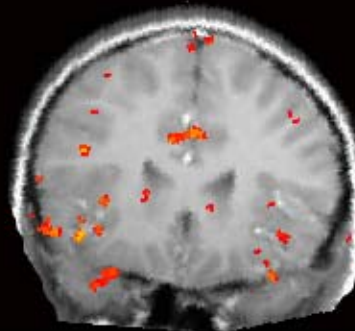
Activation during No-Go blocks in controls off-Ritalin



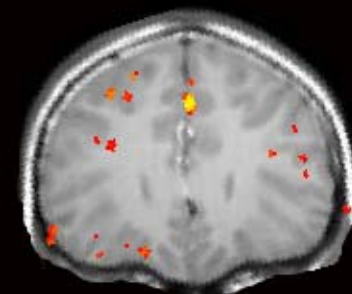
+5



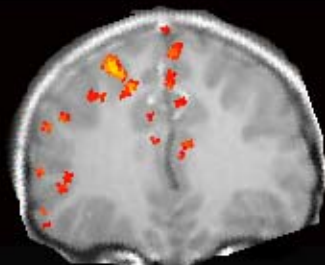
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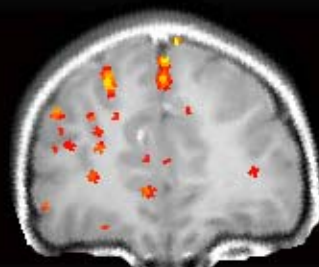
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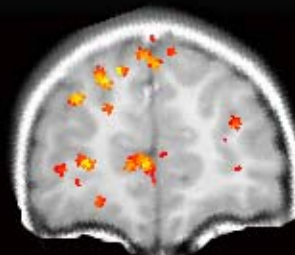
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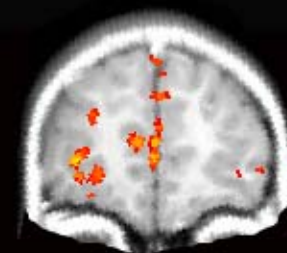
+33



+40



+47



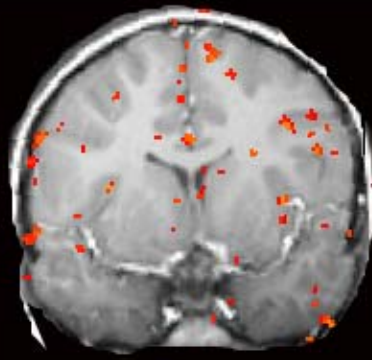
+54

$z = 1.96$

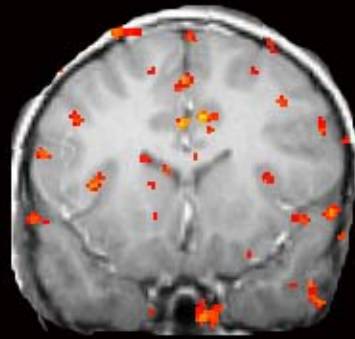


max

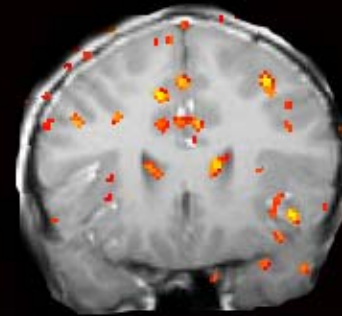
Activation during No-Go blocks in controls on-Ritalin



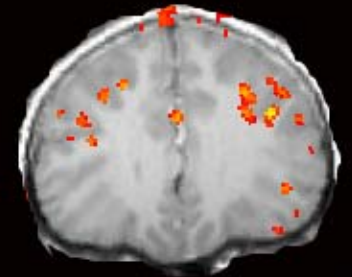
+5



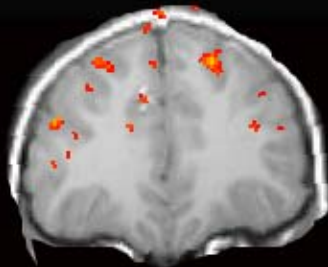
+12



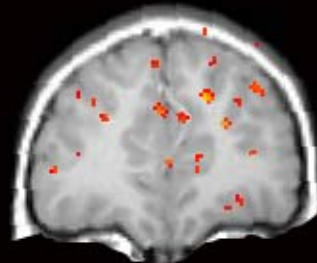
+19



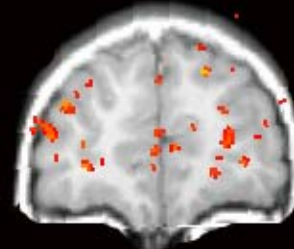
+26



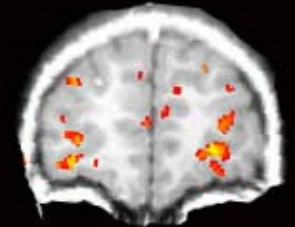
+33



+40



+47



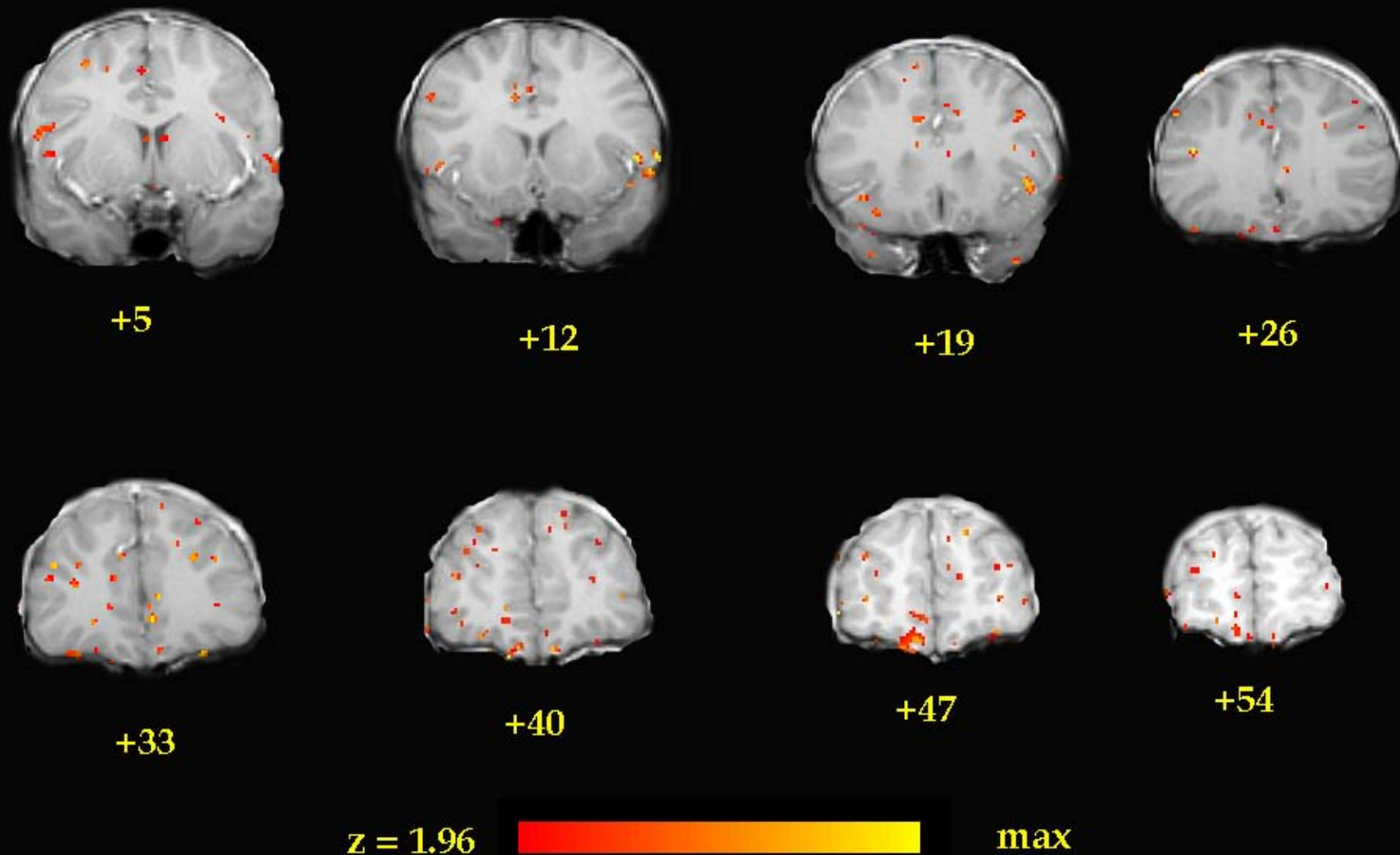
+54

$z = 1.96$

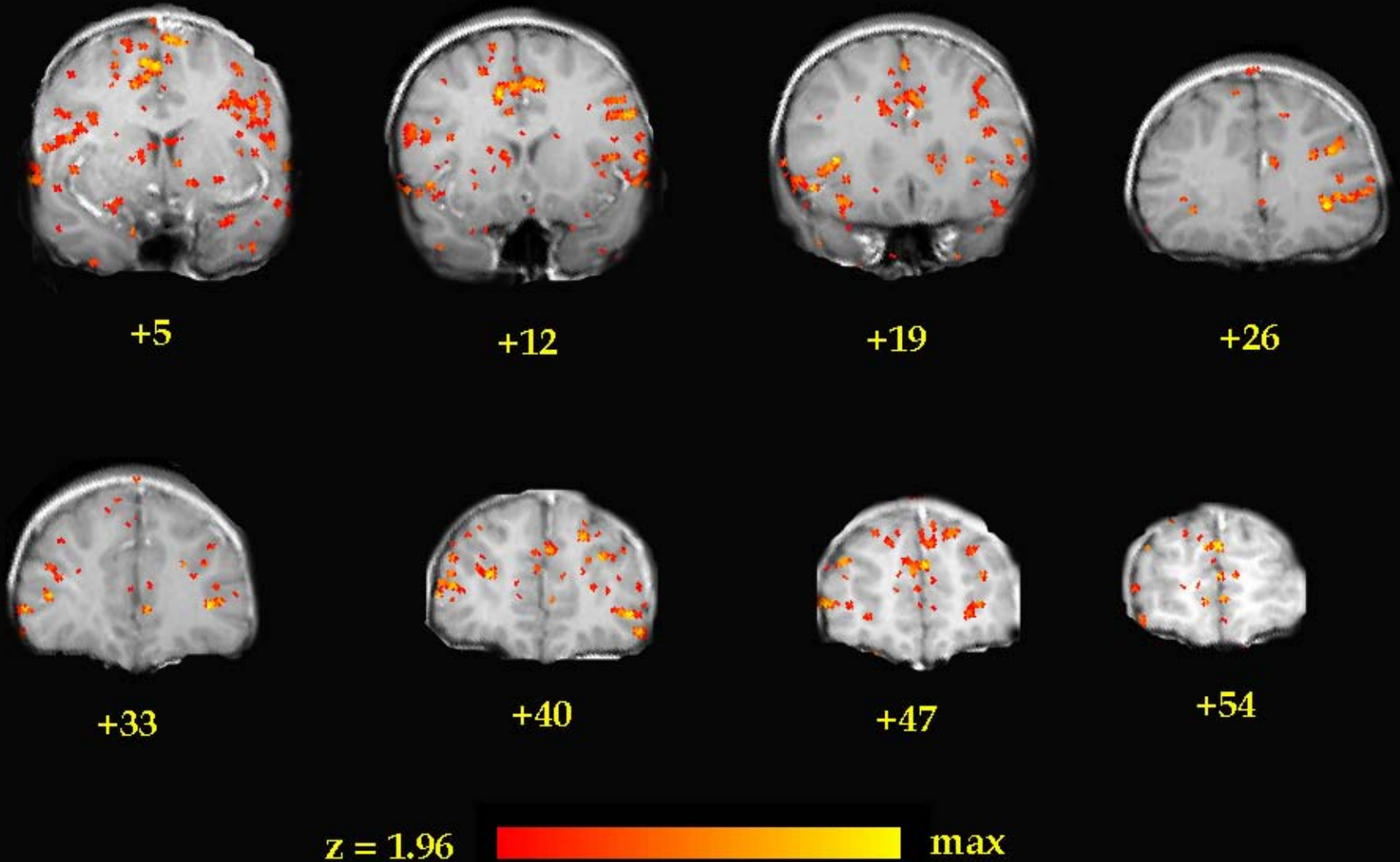


max

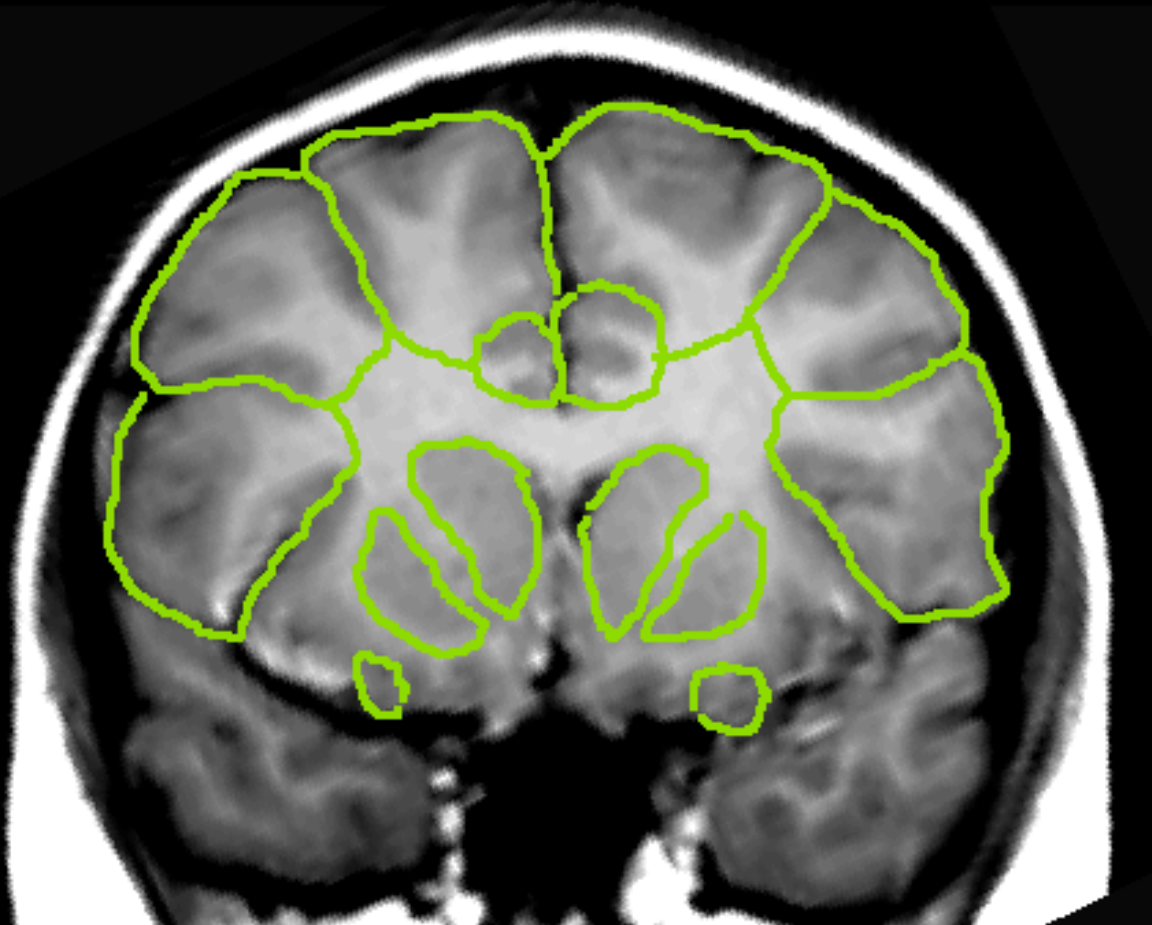
Activation during No-Go blocks in ADHD off-Ritalin



Activation during No-Go blocks in ADHD on-Ritalin



Regions of Interest



slice +12

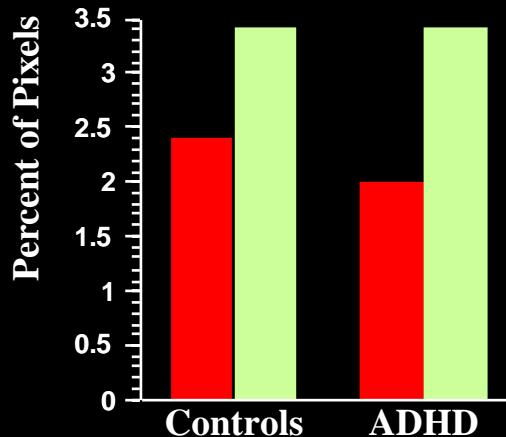
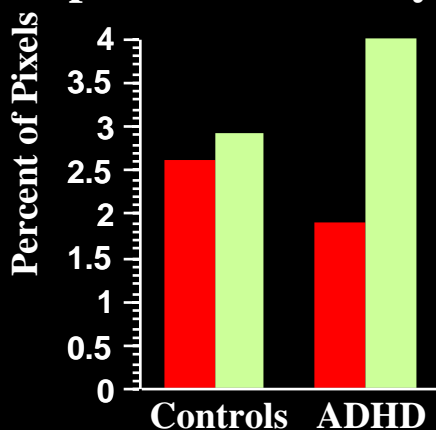
Frontal Lobe Regions

Ritalin

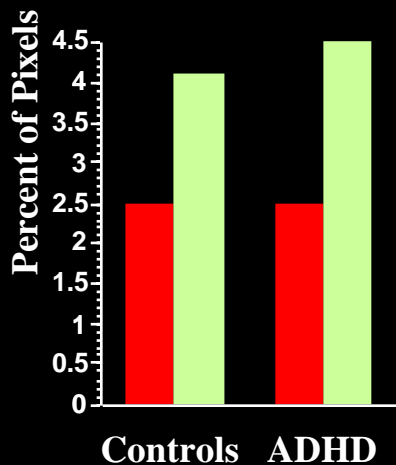
Middle Frontal Gyrus

OFF
ON

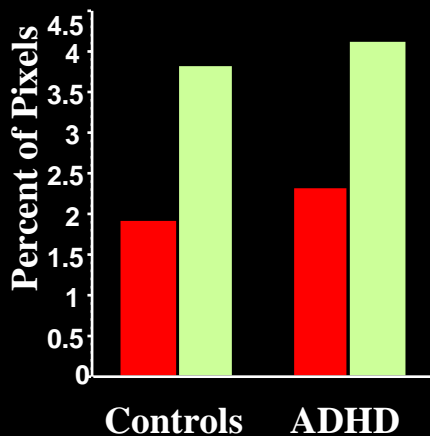
Superior Frontal Gyrus



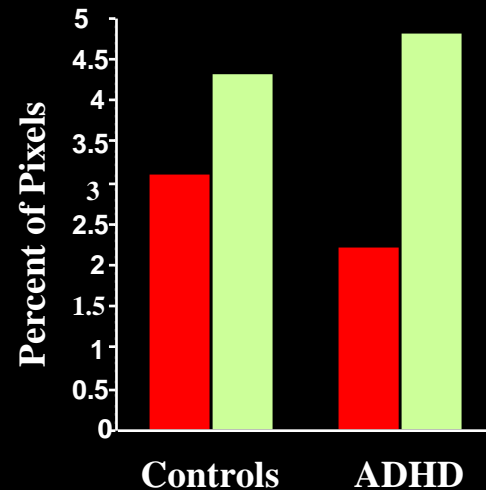
Inferior Frontal Gyrus



Orbital Frontal Gyrus



Ant. Cingulate Gyrus



Brain structures implicated in ADHD

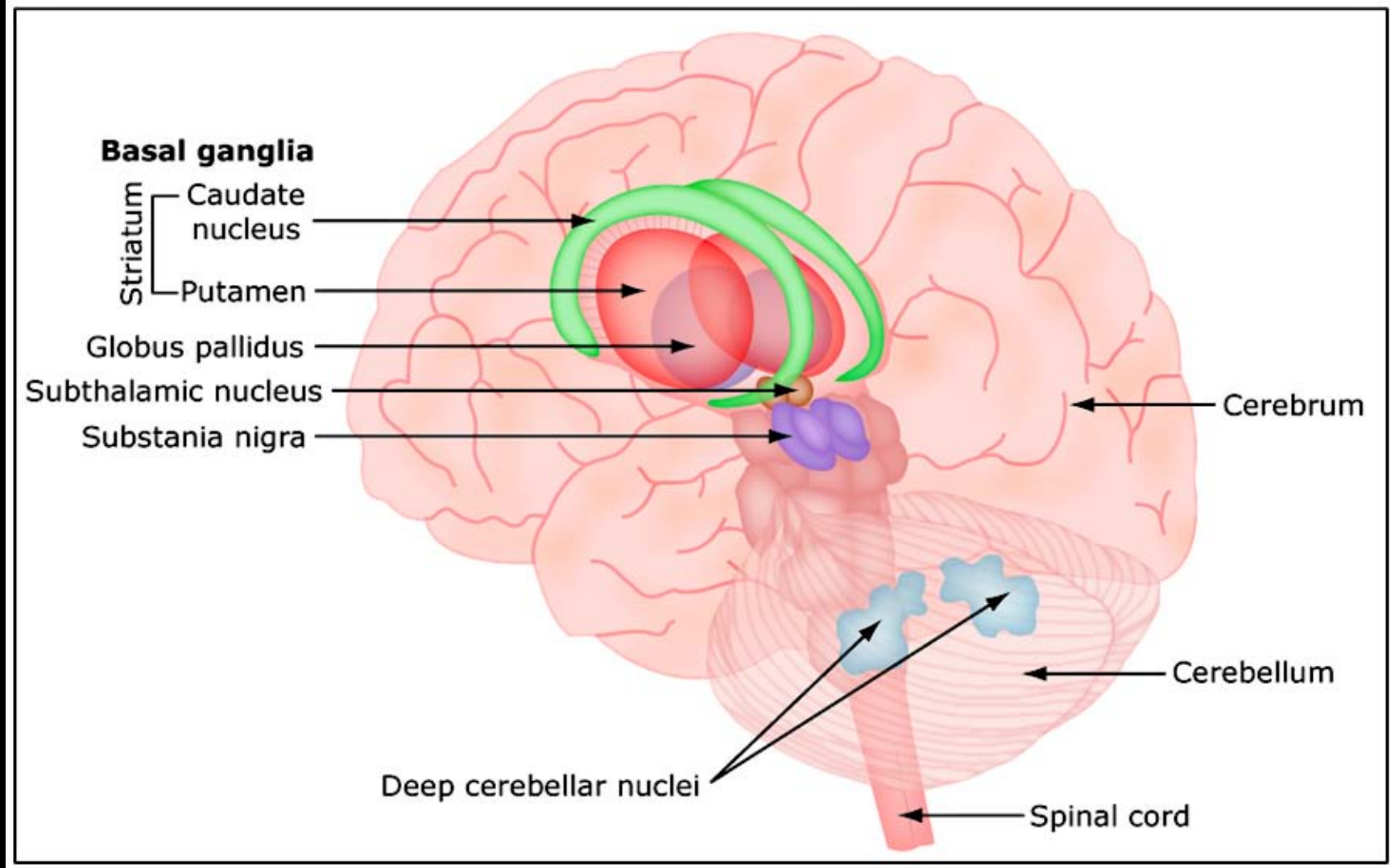
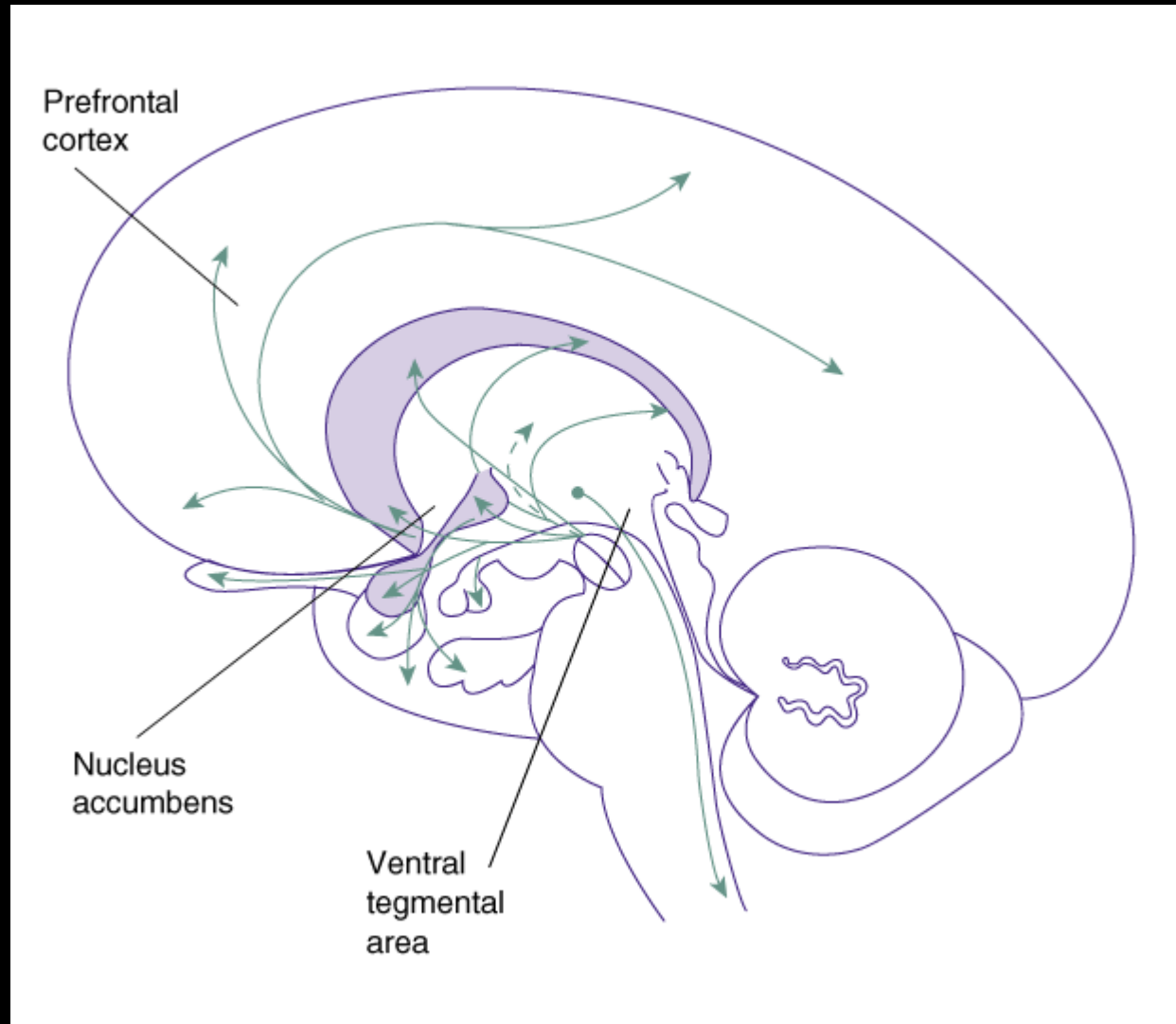
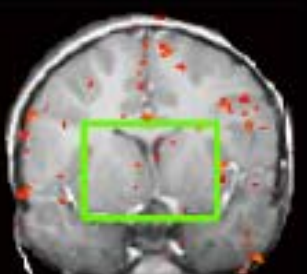
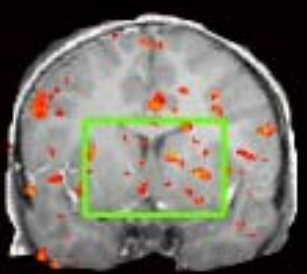
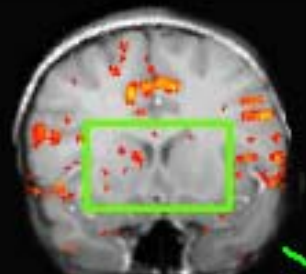
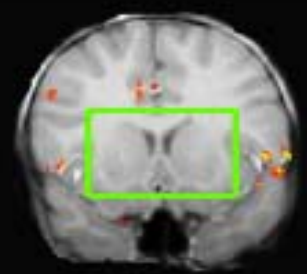
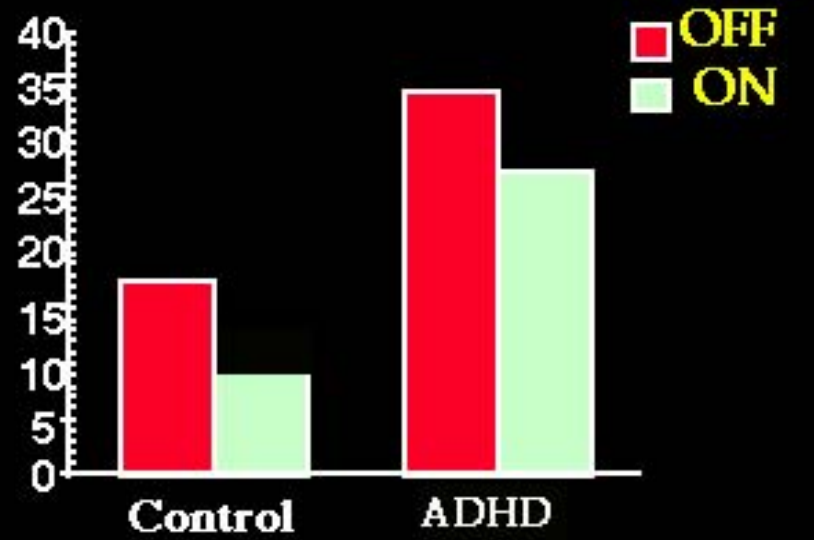
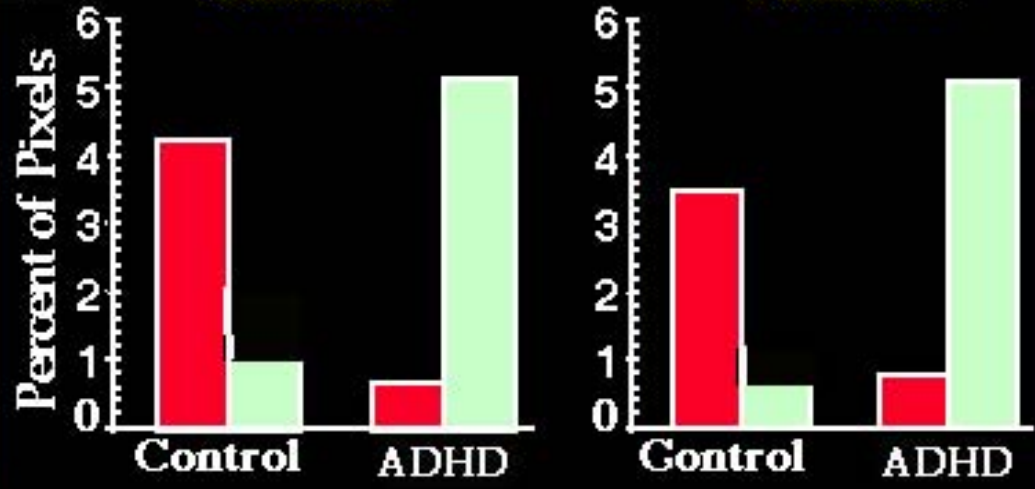


Image by MIT OpenCourseWare.

Dopaminergic pathways



A**Brain activation during impulse control****OFF-RITALIN****ON-RITALIN****ADHD****Control****C Errors in impulse control****Percent False Alarms****B****Caudate****Putamen****Percent of Pixels**

FROM VARIATION TO DISEASE

to what extent is variation “pathologized”?
how should people pursue happiness?

- height and human growth hormone?
(men, 5'9"; women 5'4")
- sadness to depression?
- shyness to social anxiety disorder?
- failure to follow directions to ADHD?

- use of stimulants to enhance performance – 7% of university students? 20% of scientists in on-line poll

- ethics – what is the right thing? also fairness, freedom, long-term risks?

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9.00SC Introduction to Psychology
Fall 2011

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