

# **Substance Abuse in Your Patients: Beyond What is Taught in Your Residency**

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## **Clinical Implications and Applications of Advances in Addiction Research to the Evaluation and Treatment of Adolescents**

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# Learning Objectives

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What does research tell us about:

- Developmental pathways and neurobiological underpinnings of adolescent addiction?
- Common co-occurring disorders ?
- Assessment and treatment ?

What are the clinical implications of addiction research?

# Resilience

Verbal IQ; school performance;  
hobby; empathic gatekeeper,  
second chance

Experimentation (90%) → SUD  
(drug 2-9%; alcohol 5-8%)

## Impedes development of :

- ✓ Coping skills
- ✓ Social /interpersonal skills
- ✓ Communication skills
- ✓ Identity, values consolidation
- ✓ Affect identification/regulation
- ✓ Self-Efficacy/external locus control
- ✓ Pro-social network

Deviant, drug involved

Failure; truancy

SUD, abuse, neglect

Individual

ODD

ADHD

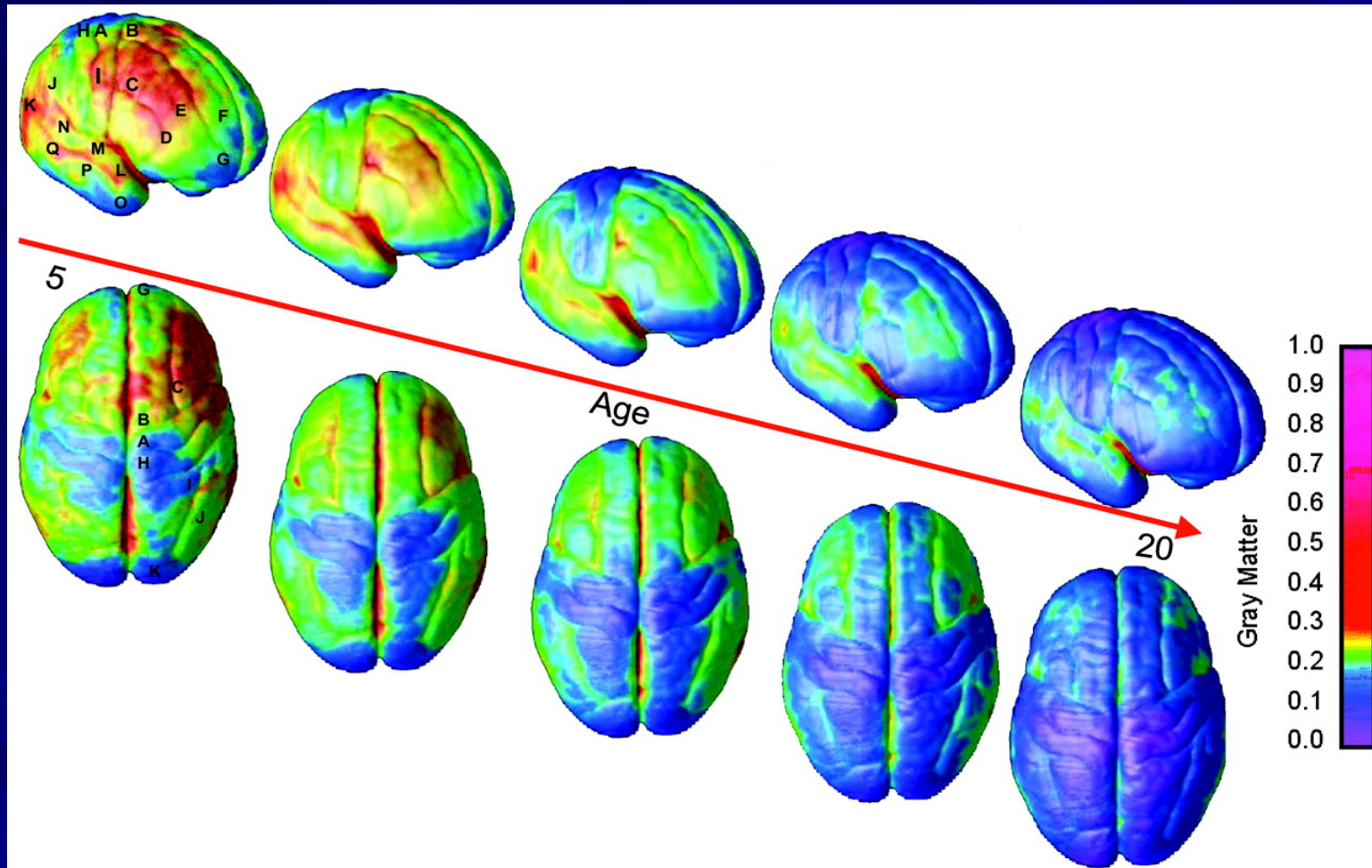
CD

ASP

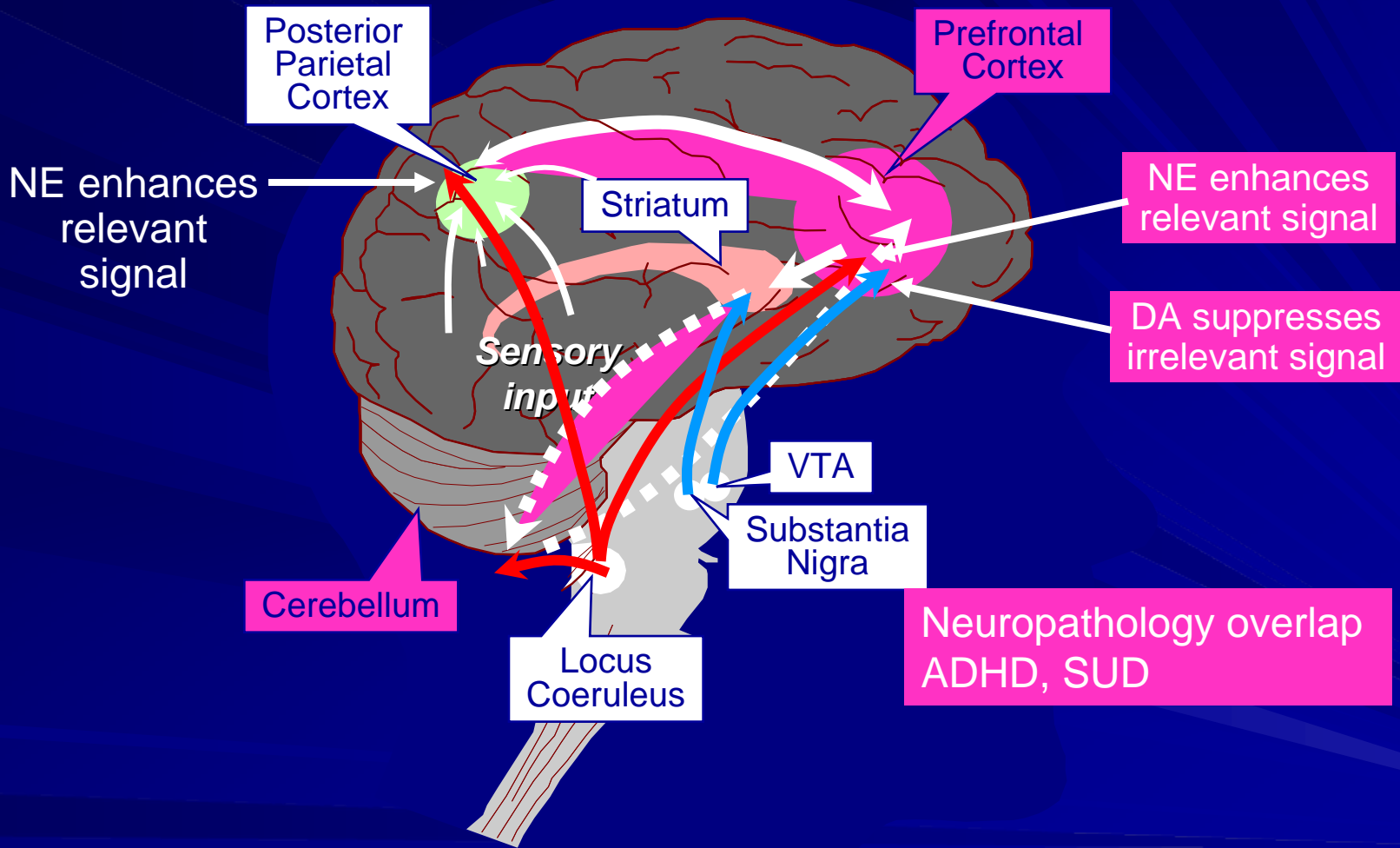
Temperament and  
co morbidity

Mood / Anxiety

# Gray Matter Development



# Brain Mechanisms in ADHD





**Comorbidity**

**Prevalence**



**risk SUD**

**Effective Tx**

**Tx with SUD**

**ADHD**

**30-50%**

**vs 10%**

**Yes**

**Stimulants**  
**Lower abuse**  
**pemoline\***  
**Atomoxetine**  
**Bupropion**  
**Modafinil\*\***

**1 RCT n=69**  
**Efficacy > PBO**  
**Good safety profile**  
**No impact on SUD**  
**absent SUD tx**

**Depression**

**15-25%**

**vs 5-7%**

**Yes**

**SSRIs\***  
**Psychotherapy**  
**CBT**  
**Interpersonal**

**1 RCT n=126**  
**\*fluoxetine + CBT**  
**for SUD**  
**Efficacy > PBO**  
**Good safety profile**

**Bipolar**

**10-15%**

**vs 1%**

**Yes**

**mood**  
**stabilizers**

**1 RCT lithium n=22**  
**Good safety profile**  
**Treats bipolar**  
**Not SUD**

**Anxiety**

**15-35%**  
**vs 5-10%**

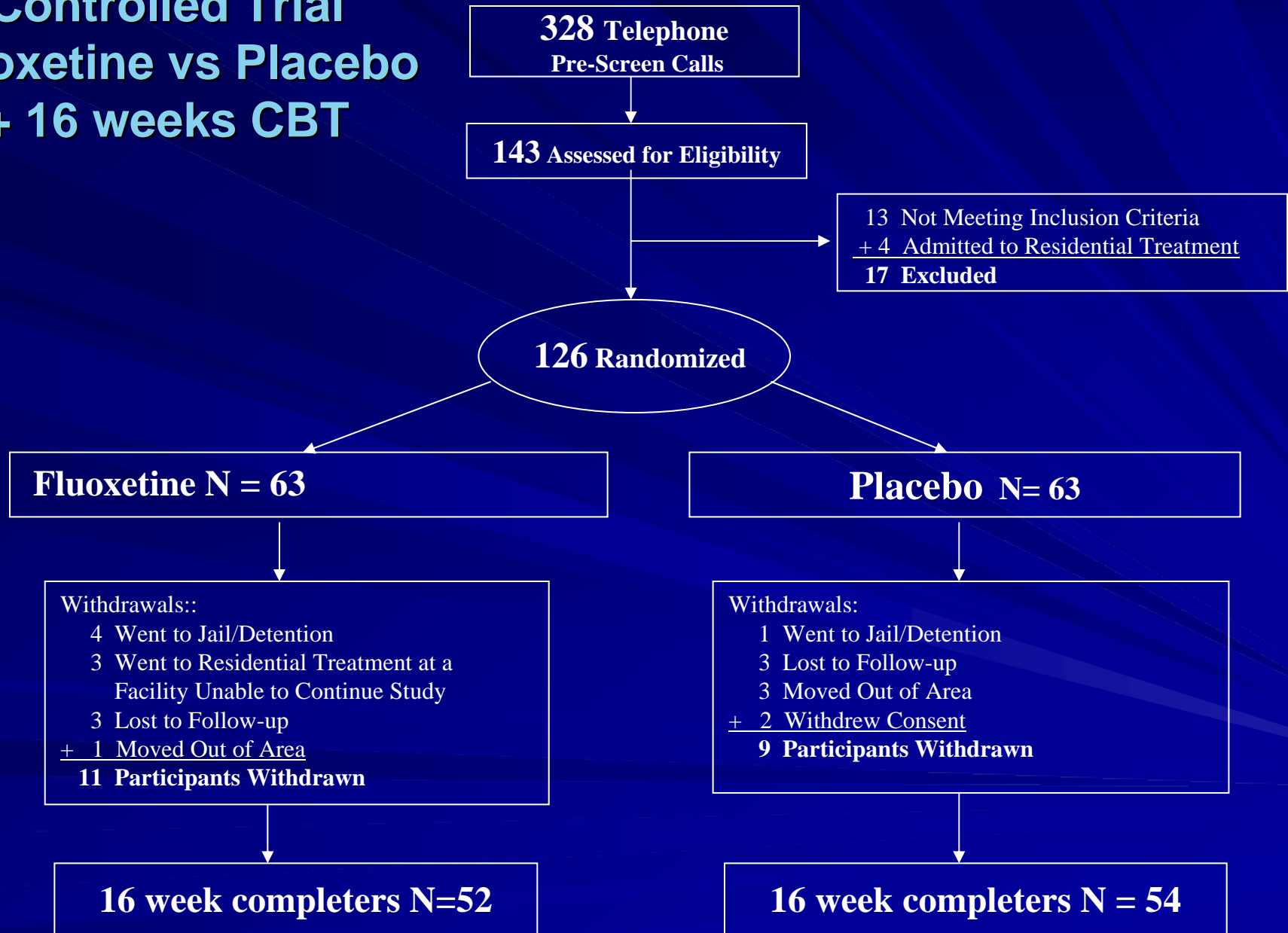
**Yes**

**SSRI /CBT**

**No RCTs**

# Randomized Controlled Trial Fluoxetine vs Placebo + 16 weeks CBT

## Study Flow Diagram



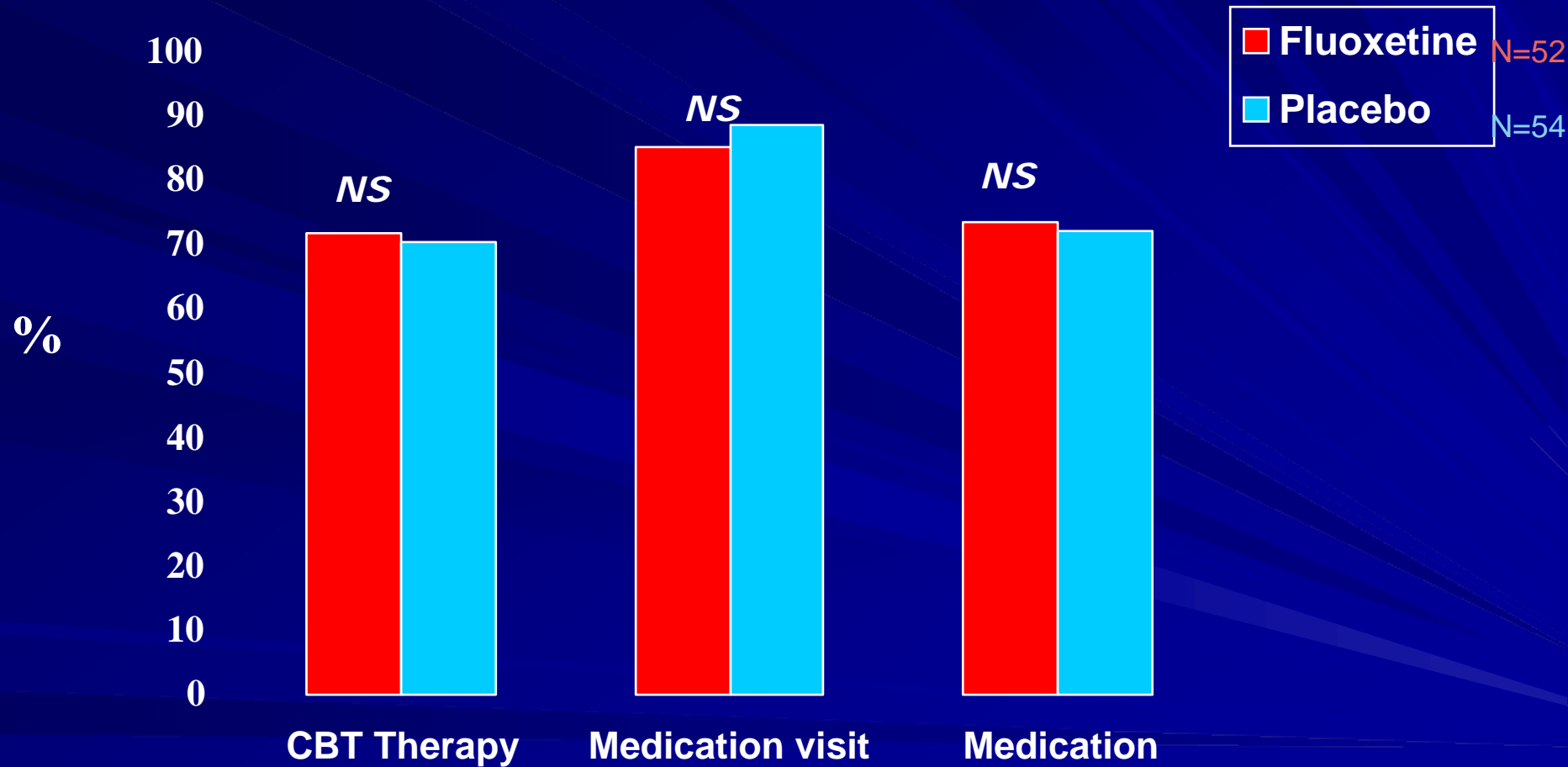
# Demographics

Demographic Characteristic		Placebo (n=63)	Fluoxetine (n=63)	Overall (n=126)
Gender n (%)	Female	20 (31.7)	21 (33.3)	41 (32.5)
	Male	43 (68.3)	42 (66.7)	85(67.5)
Age:	mean (SD)	17.02 (1.49)	17.29 (1.81)	17.16 (1.66)
Ethnicity n(%)	Caucasian	28 (44.4)	33 (52.4)	61 (48.4)
	African American	9 (14.3)	9 (14.3)	18 (14.3)
	Native American	3 (4.8)	1 (1.6)	4 (3.2)
	Asian	1 (1.6)	0 (0)	1 (0.8)
	Hispanic	17 (27.0)	17 (27.0)	34 (27)
	Other	5 (7.9)	3 (4.8)	8 (6.3)
SES: group IV category		43.98 (15.49)	44.56 (17.60)	44.27 (16.5)
Referral Source: n (%)	Court-Ordered	12 (19.0)	14 (22.2)	26 (20.6)
	<b>Non Court-Ordered</b>	51(81.0)	49 (77.8)	<b>100 (79.4)</b>

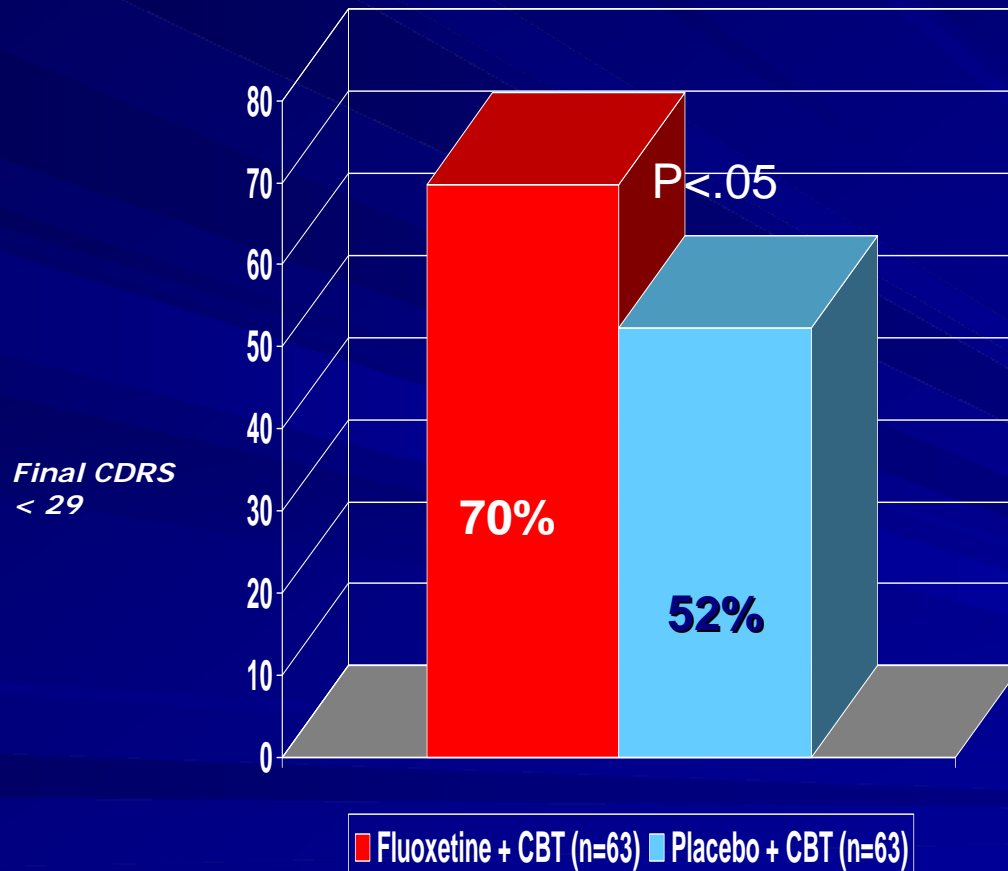


# Fluoxetine vs. Placebo

## Compliance: Medication & CBT



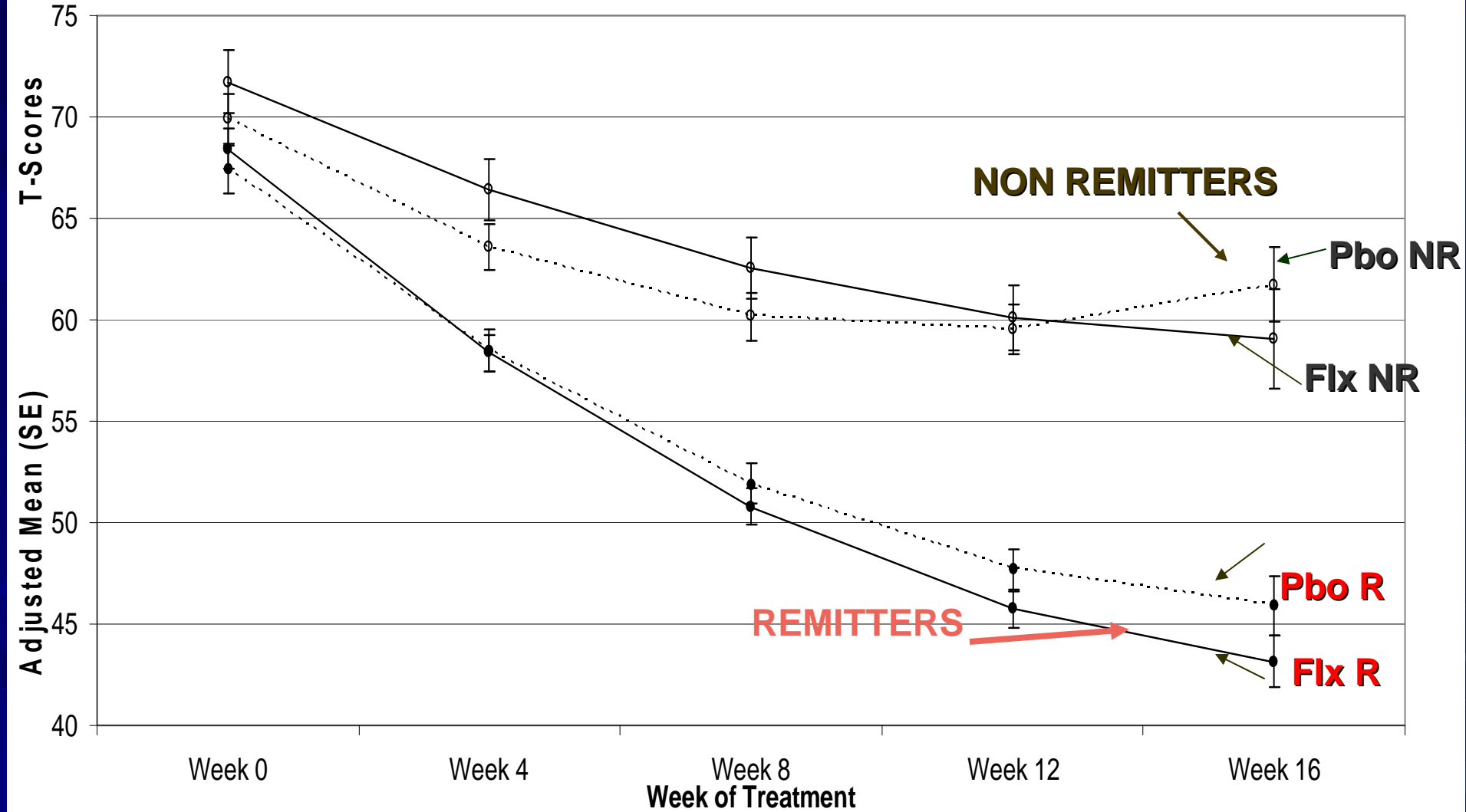
# Fluoxetine vs. Placebo Depression Remission



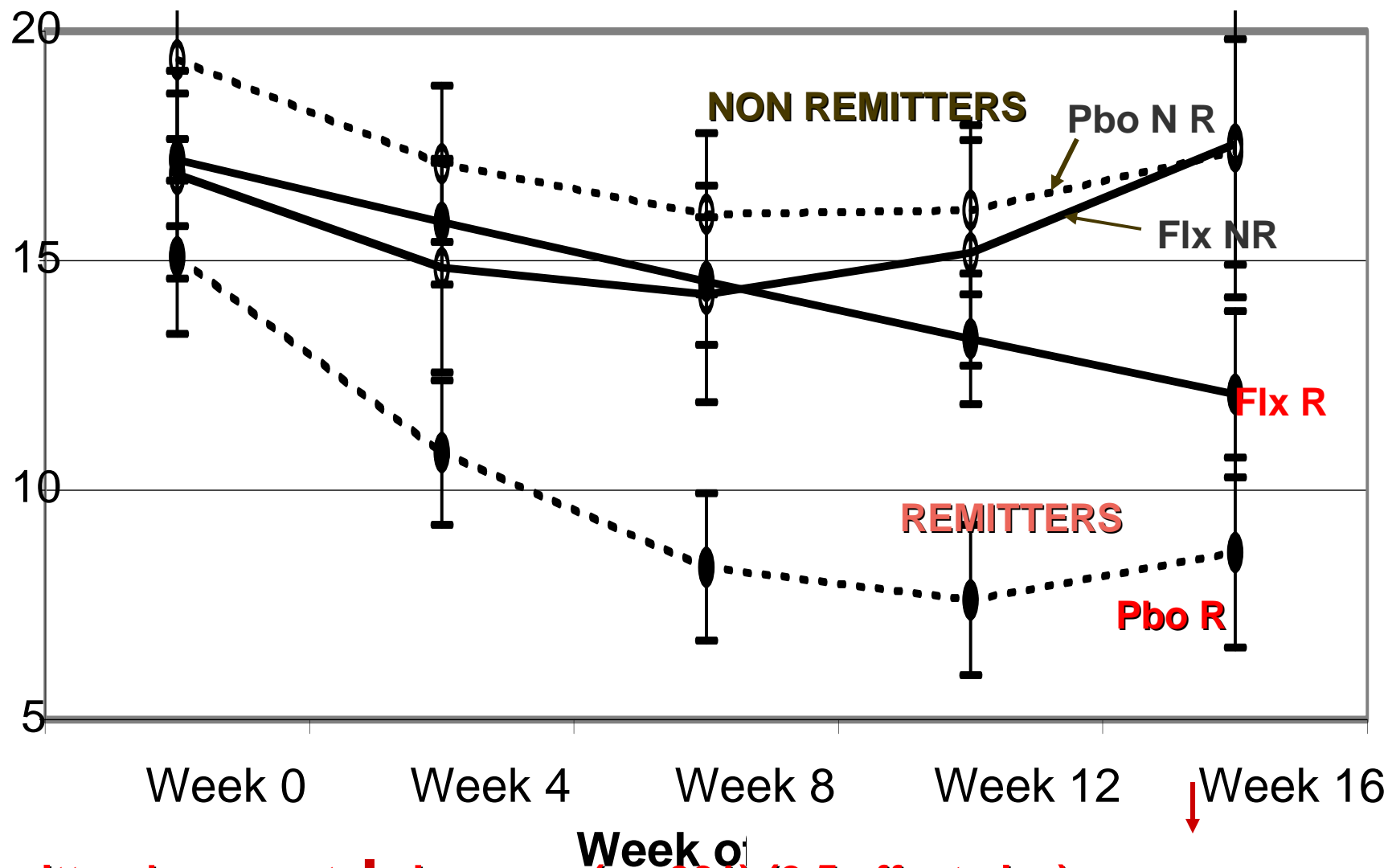
Riggs et al Archives of Pediatric and Adolescent Medicine in press

- - - ○ - - - Placebo Non-Remitter      - - - ● - - - Placebo Remitter  
 — ○ — Fluoxetine Non-Remitter      — ● — Fluoxetine Remitter

# A. Children's Depression Rating Scale-Revised T-Scores



# Change in Drug Use

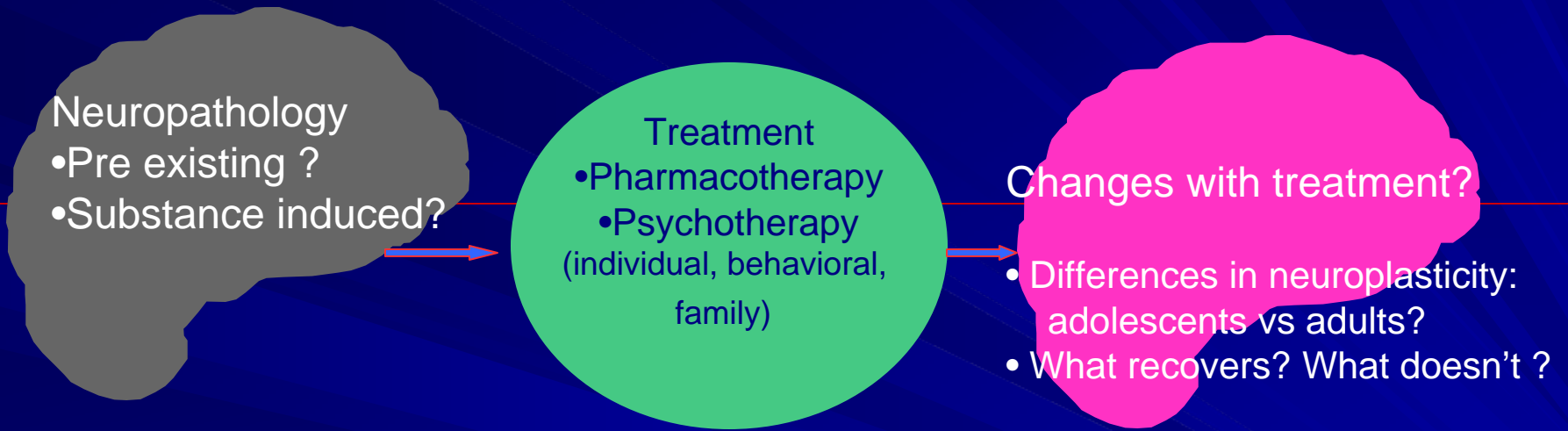


Remitters' pre post ↓ drug use ( $p < .001$ ) (0.5 effect size) (U/A R > NR  $p < .02$ )

Non-Remitters: no change in drug use (NS)

# Conclusions and Clinical Implications

- **Fluoxetine > Placebo for MDD in non-abstinent adolescents with active SUD; good safety profile**
- **Remission was better predictor of reduced drug use than medication group**
  - Remitters showed significant ↓ in drug use N
  - Non-remitters' drug use did not decrease from baseline levels
  - CBT probably active ingredient in treatment of MDD despite focus on SUD, not depression
- **Increased access to treatment (80% not court-mandated)**
- **Empirical support for integrated SUD/mental health tx**
  - Depression outcomes as good or better than controlled trial in depressed teens without SUD
  - Change in drug use, compliance, retention as good or better than substance treatment in adolescents without comorbidity / < severe psychopathology



### Neuropathology

- Pre existing ?
- Substance induced?

### Treatment

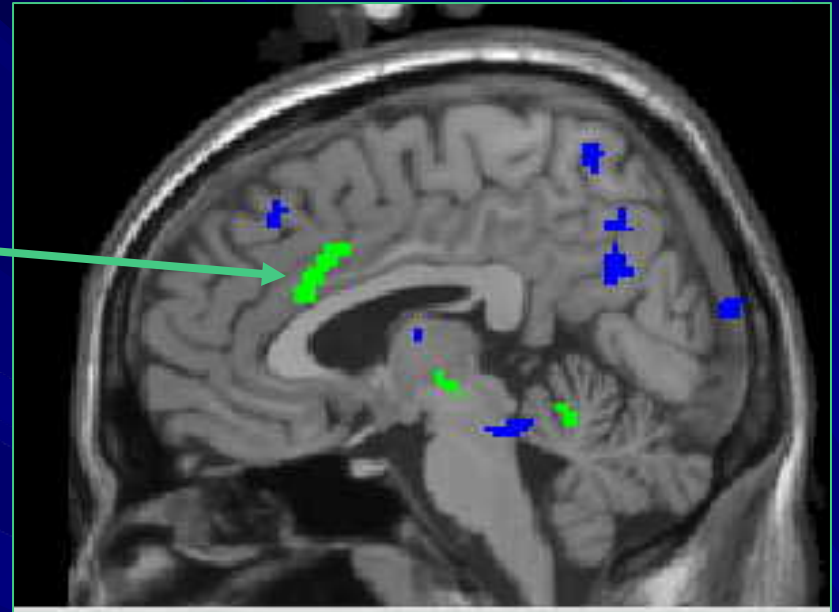
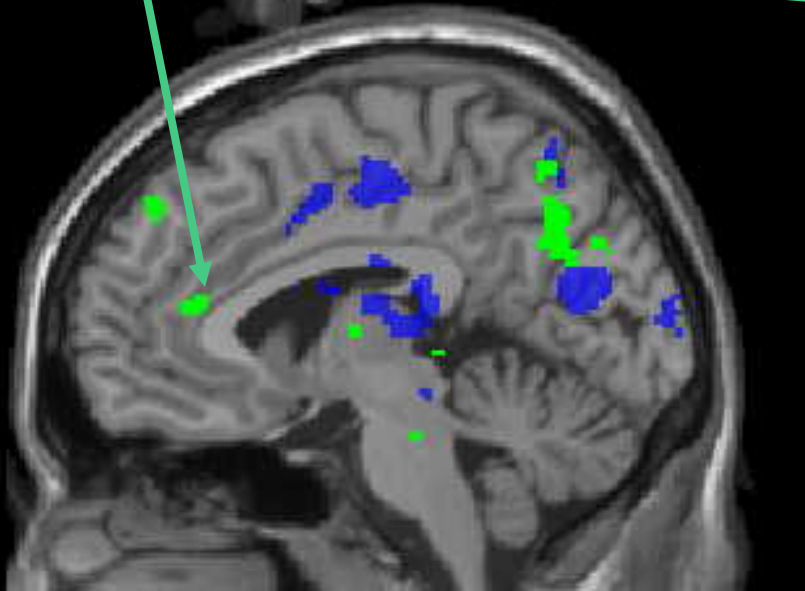
- Pharmacotherapy
- Psychotherapy  
(individual, behavioral,  
family)

### Changes with treatment?

- Differences in neuroplasticity:  
adolescents vs adults?
- What recovers? What doesn't ?

**On STROOP test:**

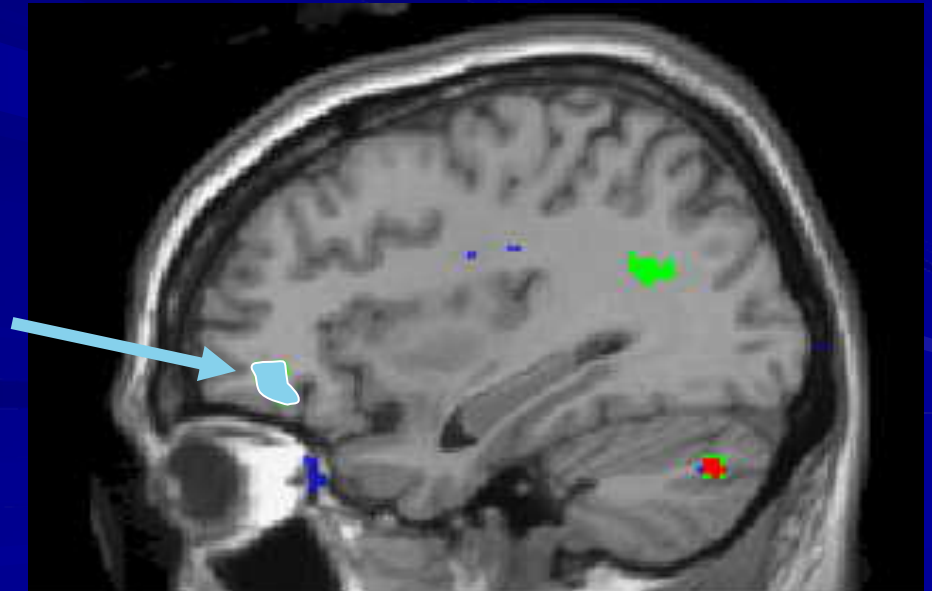
Substance dependent adolescents exhibited activation in the **rostral & caudal ACC...**



...and R orbito-frontal cortex (OFC)

**Non-dependent controls did not**

.....but are differences pre-existing or caused by drug use?



# Greater Pretreatment Brain Activation Drug > Food

- **Ventral Tegmentum**
- **Nucleus accumbens**
- **Amygdala**
- **Thalamus**
- **Anterior Cingulate**
- **Medial frontal cortex**
- **Midbrain**
- **Posterior visual cortex**
- **Cerebellum**



Preliminary results in 11 adolescents with cannabis and other substance use disorders suggests greater activation of reward circuit in response to drug cues than food before treatment

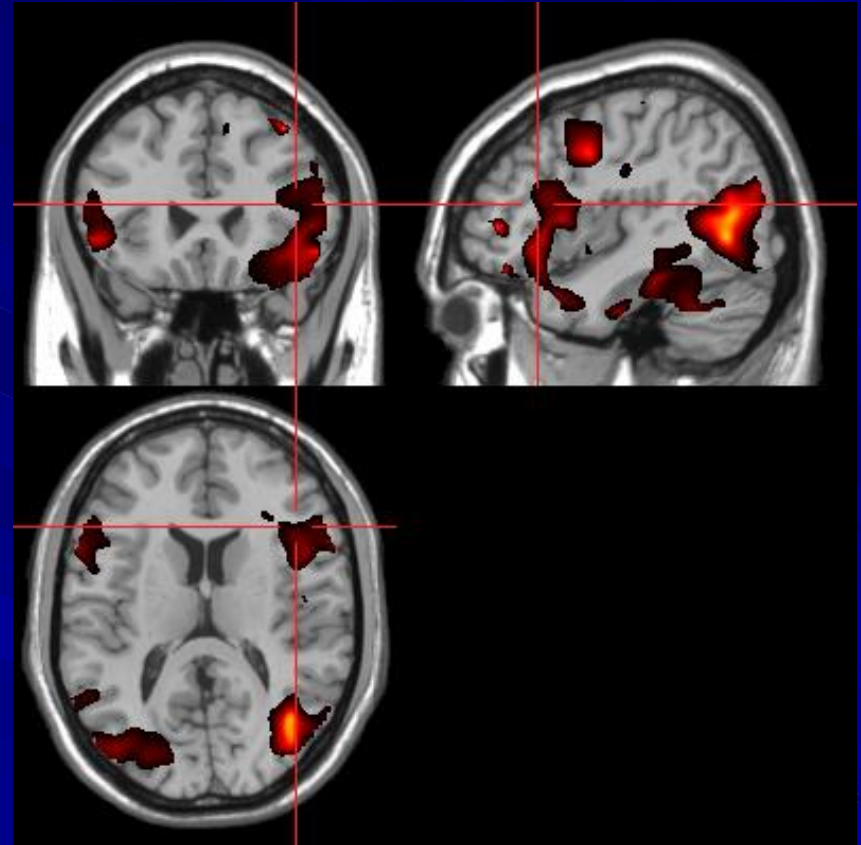


# Greater post-treatment activation Drug > Food in areas of cognitive control\* compared to pre-treatment

(n=10 post scans; n=6 valid;  $p < .01$ )



Pretreatment



Post-treatment

\* ACC and cortical regions --medial frontal, lateral inferior frontal, dorsolateral, prefrontal

# Clinical Implications

## Directions for future research

- Decrease barriers to treatment access
- Expand integrated /coordinated continuum of care  
( medical, psychiatric, substance treatment)
- Earlier interventions & improved continuing care
  - school based, indicated prevention
  - parity for mental health and SUD treatment
  - utilization of existing community based resources
  - Relapse Prevention : build “internalized motivation  
“ to maintain treatment gains by involvement in  
positively rewarding activities incompatible with drug  
use during treatment



# Clinical Implications

## Directions for Future Research

### Medication Development

- Monotherapy better than polypharmacy
- Clinical trials using medications that target both SUD and comorbidity such as bupropion
  - controlled trials support efficacy for ADHD, MDD, nicotine dependence
  - reducing methamphetamine craving and use

