

# **Anorexia Nervosa: What's New about an Old Illness?**

B. Timothy Walsh MD

Columbia University

New York State Psychiatric Institute

# Conflict of Interest Disclosure

In the last 12 months, Dr. Walsh has received research support from:

AstraZeneca

# The plan...

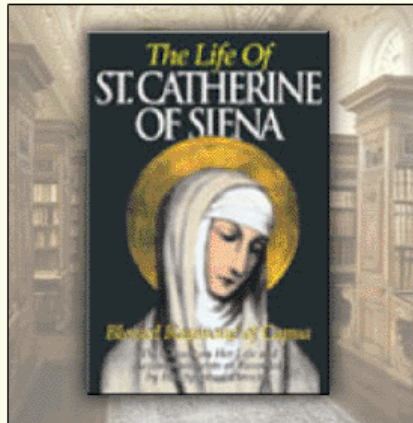
- Review the basics, including DSM-5
- Very brief update on epidemiology and treatment
- The enigma of persistence:
  - A new model

# Acknowledgements

**Too many thank you's to list, but include:**

- experimental subjects
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- Eating Disorders Research Unit at  
Columbia/NYS Psychiatric Institute  
(esp. Joanna Steinglass)

# Anorexia Nervosa: An Old Illness



1350 St. Catherine of Siena

Holy Anorexia?

1689 Richard Morton

“Nervous Consumption”

1874 William Gull

“Anorexia Nervosa”

1873 Charles Leseque

“Hysterical Anorexia”

# **Anorexia Nervosa**

## **Key Diagnostic Features**

- Relentless pursuit of thinness
- Fear of becoming fat
- Significantly underweight

# DSM-5: ANOREXIA NERVOSA

- A. Restriction of energy intake relative to requirements leading to a significantly low body weight in the context of age, sex developmental trajectory, and physical health. *Significantly low weight* is defined as a weight that is less than minimally normal, or, for children and adolescents, less than that minimally expected.
- B. Intense fear of gaining weight or becoming fat, **or persistent behavior to avoid weight gain**, even though at a **significantly low weight**.
- C. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body shape or weight on self-evaluation, or **persistent lack of recognition** of the seriousness of current low body weight.

**Current** subtype: Restricting vs. Binge/Purge

# Anorexia Nervosa

## Associated Features

### Behavioral

Obsession with food  
Peculiar eating  
Binge eating  
Laxative/diuretic abuse  
Compulsive behavior  
Depression  
Social isolation  
Increased physical activity

### Physiological

Hypothermia, bradycardia,  
hypotension  
Lanugo  
Edema  
Anemia, leukopenia  
Increased LFT's  
Low estrogen, LH, FSH  
Low-normal T4  
High cholesterol  
Decreased brain mass  
Osteoporosis



## Minnesota "Starvation" Experiment 1944



LIFE

# **Anorexia Nervosa: Long-Term Outcome**

- **Full Recovery:** 1/3 to 1/2
- **Death:** 5% per decade of follow-up
- **Alive but not well:** the rest
- **Obesity?:** rare

# Epidemiology of Anorexia Nervosa

- Lifetime prevalence among females 1-2%.
- 12 month prevalence ~0.5%.  
~1/10<sup>th</sup> as frequent among males.
- Incidence (# new cases/year) has probably *not* changed *dramatically* in the last 40 years.

# Treatment Update

# Treatment of Anorexia Nervosa

- Weight Gain is Essential

~4000 kcals above maintenance per pound gained

Intensive & structured care usually successful

Parenteral methods rarely needed

- Psychotherapy?

- Medication?

# Anorexia Nervosa

## Proposed Treatments

- Thyroid Hormone
- ACTH
- Lobotomy
- ECT
- Chlorpromazine
- + Insulin
- Amitriptyline
- Lithium
- Phenoxybenzamine
- Domperidone
- THC
- Cyproheptadine
- Fluoxetine
- Olanzapine
- Psychoanalysis
- Individual therapy
- Family therapy
- Behavior therapy

**Therefore,  
controlled studies  
are essential!**

# **Anorexia Nervosa: Psychological Treatment**

- **For younger patients:**  
the 'Maudsley' method
- **For older patients:**  
CBT?  
Non-specific clinical management?

# The 'Maudsley' Intervention

Russell et al, 1987; Lock et al, 2001; Lock & leGrange, 2005

- Outpatient weight-gain treatment
- Twenty sessions over 6-12 months
- Puts the PARENTS in charge of the refeeding process (appropriate control, ultimately relinquished), contrary to traditional clinical recommendation of “parentectomy”
- Makes no assumption about etiology of AN



# TREATMENT MANUAL

## for Anorexia Nervosa

*A Family-Based  
Approach*

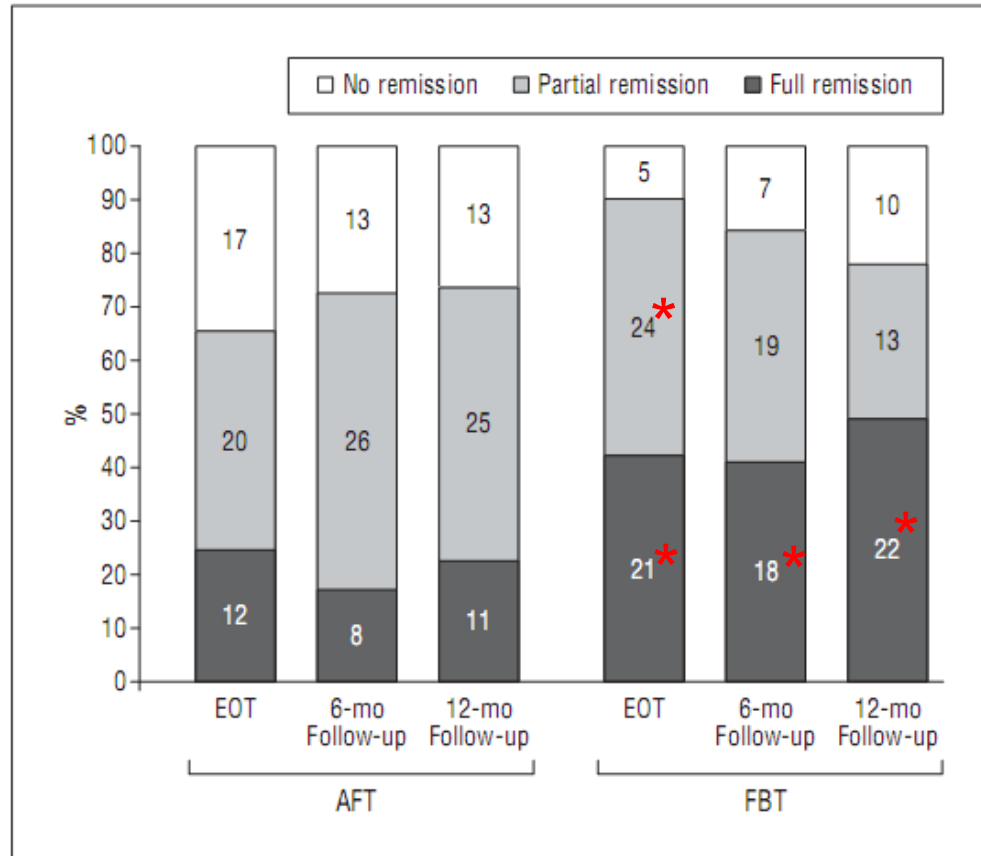
**JAMES LOCK  
DANIEL LE GRANGE  
W. STEWART AGRAS  
CHRISTOPHER DARE**

# HELP YOUR TEENAGER BEAT AN EATING DISORDER

- Learn why you need to act now.
- Find out what the research says about which treatments work.
- Take charge of changes in eating habits and exercise.
- Put up a united family front to prevent relapse.

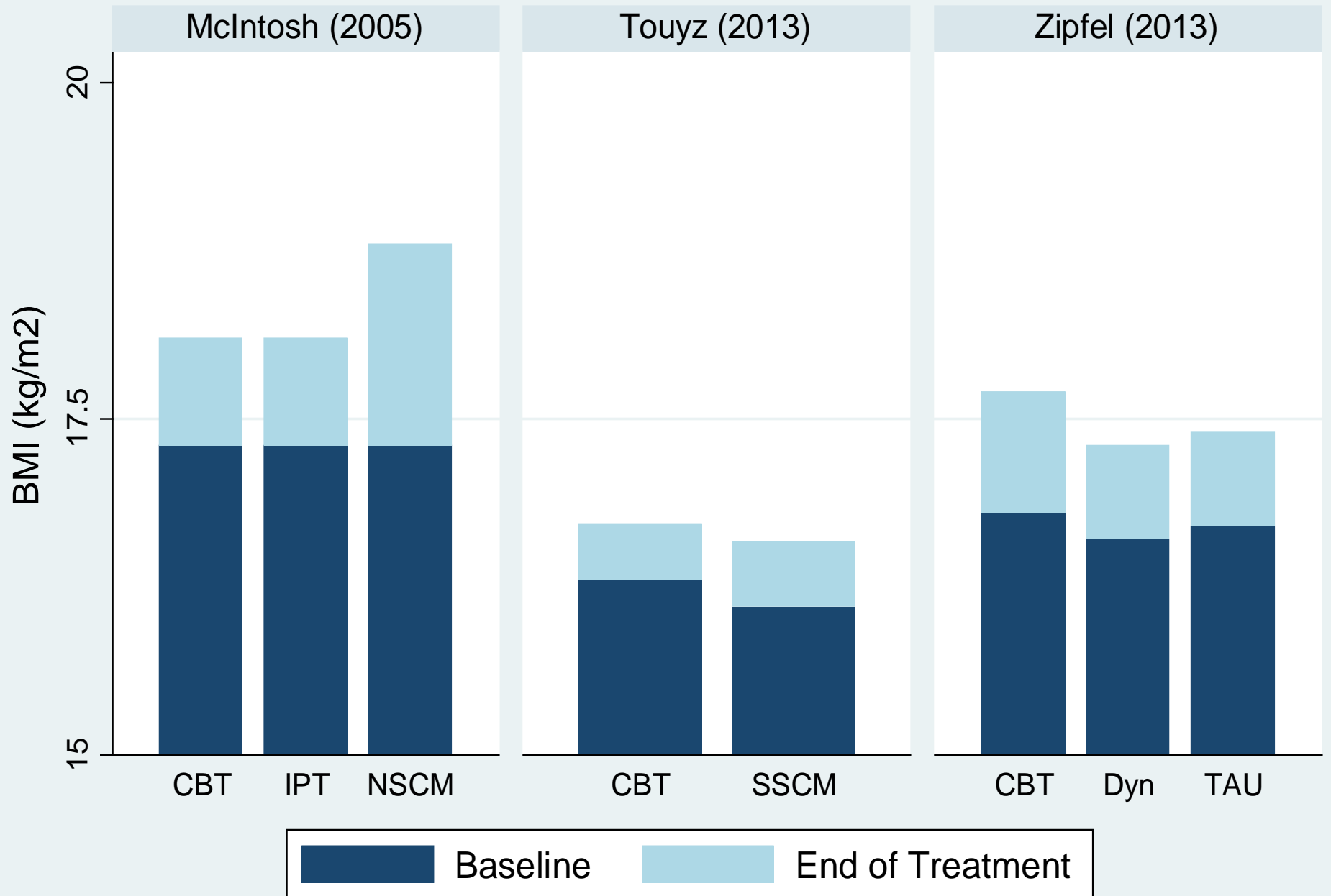
**JAMES LOCK, MD, PhD  
DANIEL LE GRANGE, PhD**

# Treatment of Adolescents: “Maudsley” vs Individual Therapy



**Figure 2.** Observed partial and full remission rates by treatment assignment (end of treatment [EOT]: adolescent-focused individual therapy [AFT], n=49; family-based treatment [FBT], n=50; 6-month follow-up: AFT, n=47; FBT, n=44; and 12-month follow-up: AFT, n=49; FBT, n=45).

# Psychotherapy for Adult Outpatients with AN



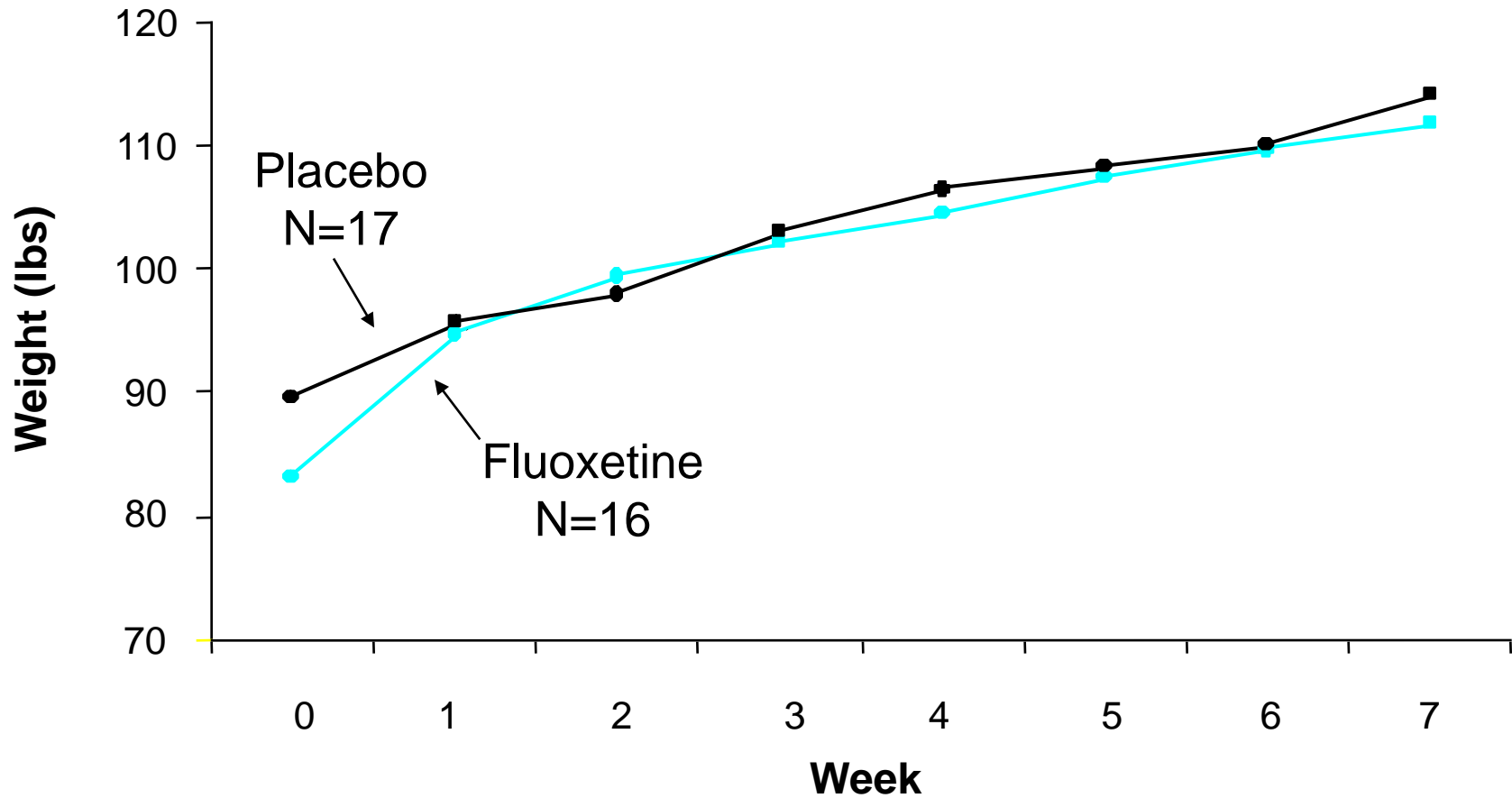
# **Anorexia Nervosa: Controlled Trials of Medication**

- Antidepressants
- Antipsychotics
- Serotonin Antagonists
- Lithium
- THC
- Cisapride
- Zinc

# Anorexia Nervosa: Controlled Trials

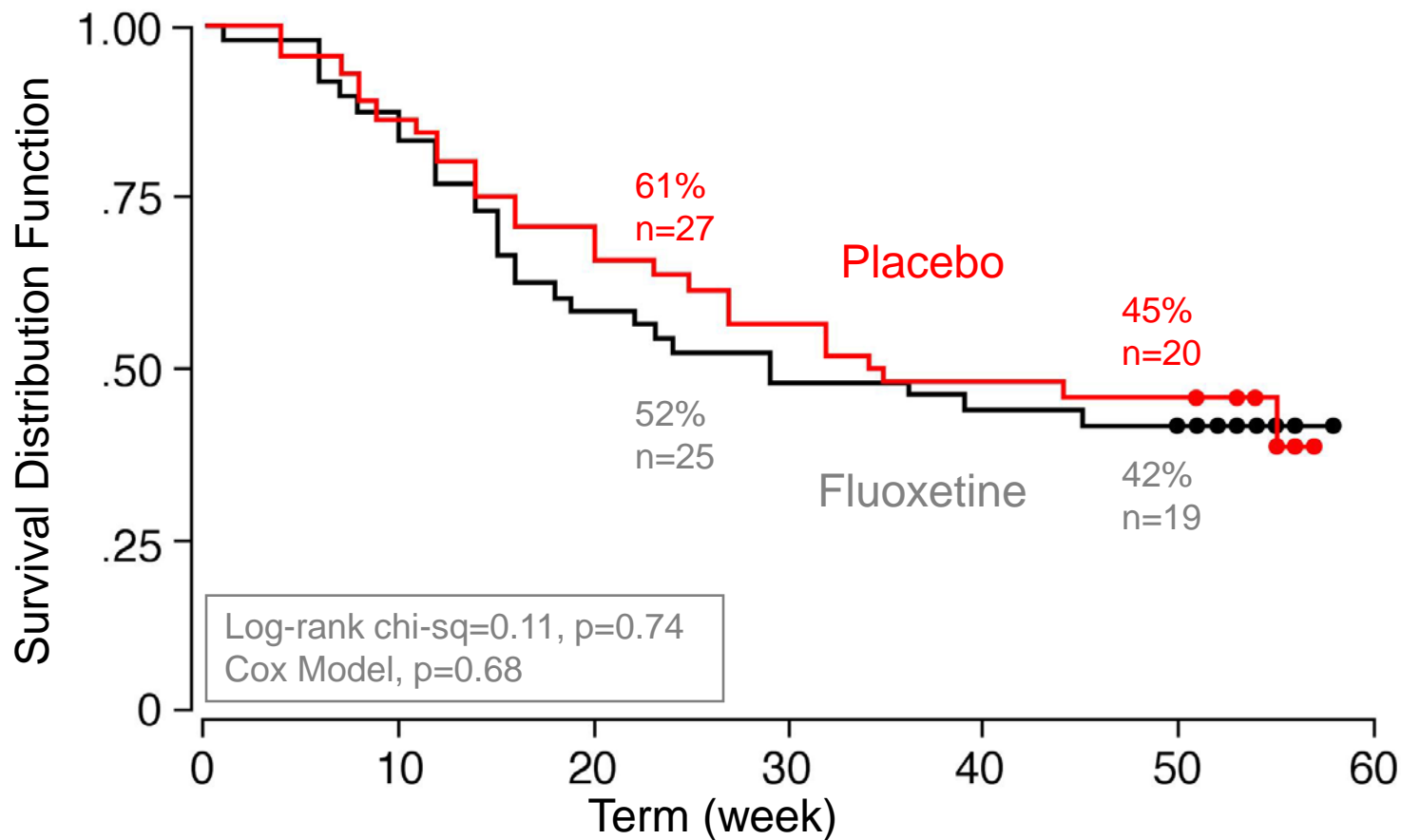
<u>Class</u>	<u># Trials</u>	<u>Medication</u>	<u>Results</u>
Antidepressant	4	CMI, AMI (2), FLX	-
Antipsychotic	2	Sulpiride, Pimozide	-
	4	Olanzapine	+
Serotonin Antagonist	3	Cyproheptadine	+/-
Lithium	1		-
THC	1		-
Cisapride	1		+/-
Zinc	3		+/-

# Fluoxetine vs. Placebo in Anorexia Nervosa



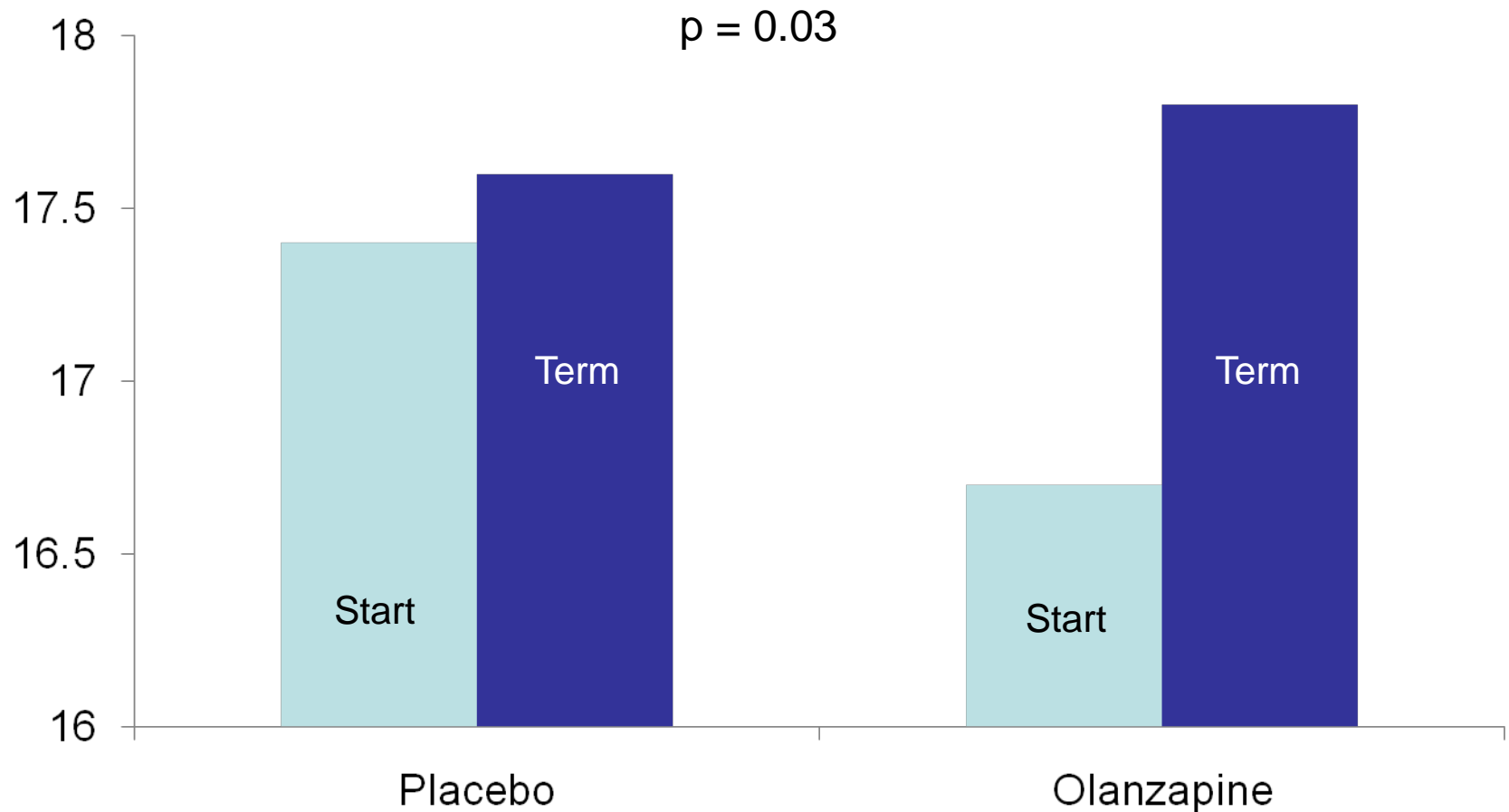
Attia et al, 1998

# Anorexia Nervosa: Fluoxetine to Prevent Relapse



(Walsh, Kaplan et al, JAMA. 295:2605-12, 2006)

# Anorexia Nervosa Olanzapine vs Placebo



**Attia et al, Psychol Med, 2011.**



# Treatment of Anorexia Nervosa

## State of the Art, 2011

- For adolescents:
  - Maudsley Method
- For adults:
  - *No* impressively effective, evidence-based treatment, either psychotherapy or medication
  - Hints about possible utility of olanzapine

# **The Enigma of Persistence**

# Why is Anorexia Nervosa so difficult to treat?

- The solution to the core problem is deceptively simple:

**EAT!**

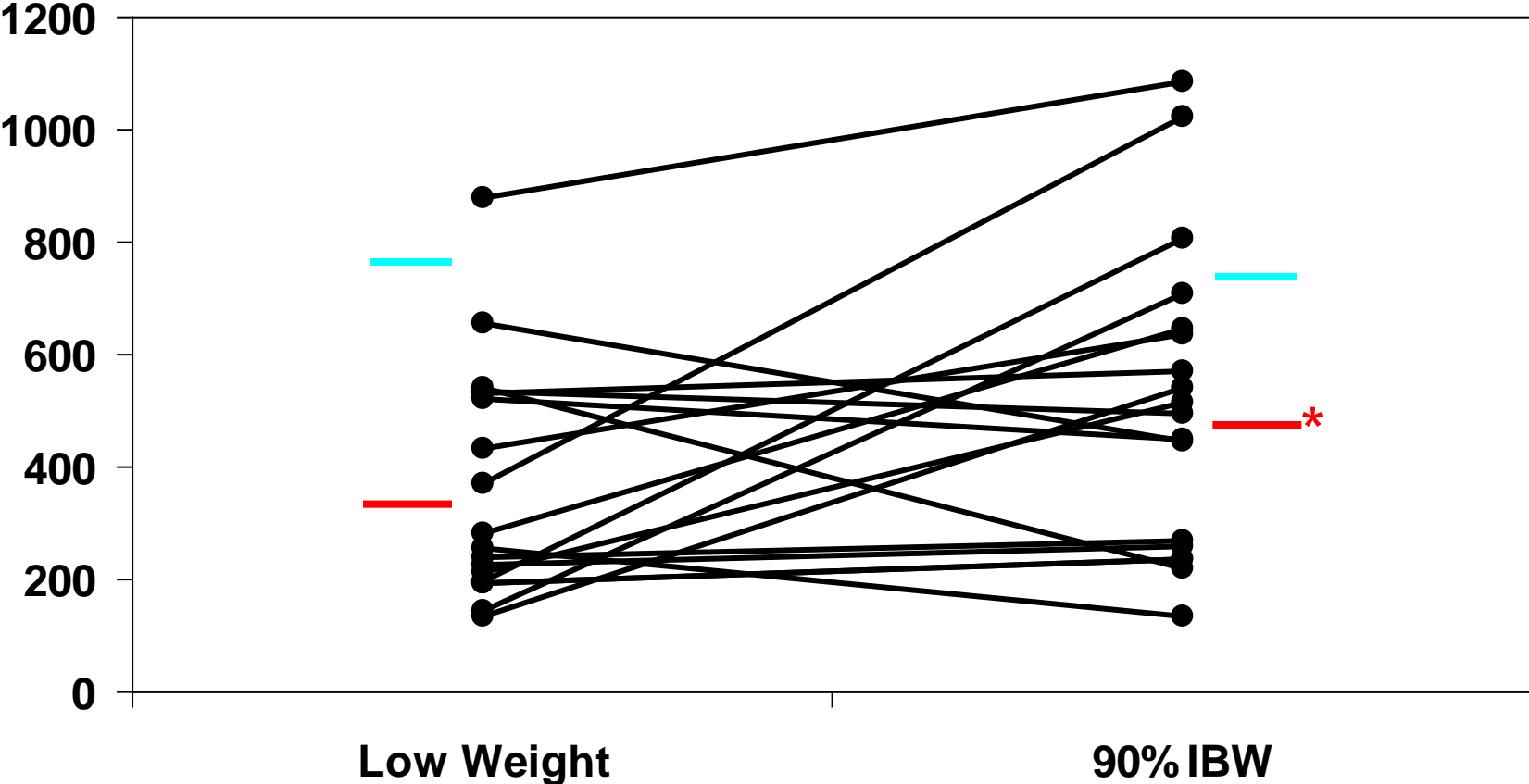
# Cognitive Neuroscience meets Anorexia Nervosa?

- The defining behavioral characteristic of Anorexia Nervosa is the avoidance of fat intake.
- This behavior can be objectively measured and is linked to clinical outcome.
- Cognitive neuroscience has learned much about the neural basis of choice.
- This knowledge can be applied to understand the neural basis of the choice to consume low-fat food in Anorexia Nervosa.

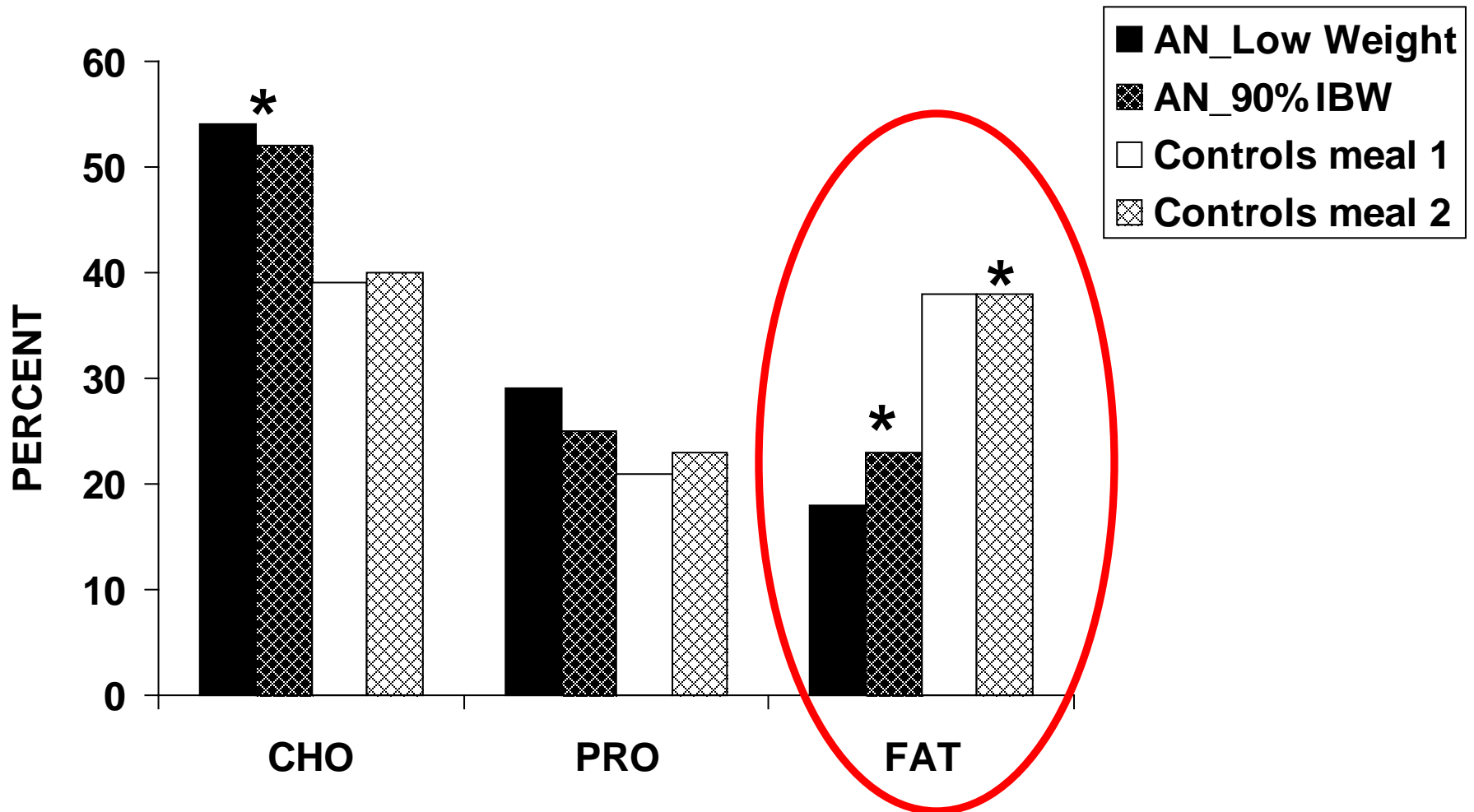
Walsh BT: The enigmatic persistence of anorexia nervosa.  
*Am J Psychiatry* 2013 170: 477-484.



# Calories consumed during Multi-Item Meals before and after weight gain



# Macronutrient Composition of Test Meal



\* CHO: significantly different from controls

FAT: significantly increases in patients but remains different from controls

# Outcome Status vs Pre-Discharge Diet Record

The pre-discharge diet records of the patients with better outcomes indicated:

- Greater energy density
  - Higher % of calories from fat
- Greater diet variety

**Suggesting:** the persistence of dieting behavior is a major contributor to the persistence of the illness.



# Persistent Behavior

- Persistent behavior that is not innate is learned via two related but distinct processes:
  - Action-Outcome learning: goal directed
  - Stimulus-Response learning: habit formation

# Action-Outcome Learning

(aka instrumental conditioning, operant conditioning)

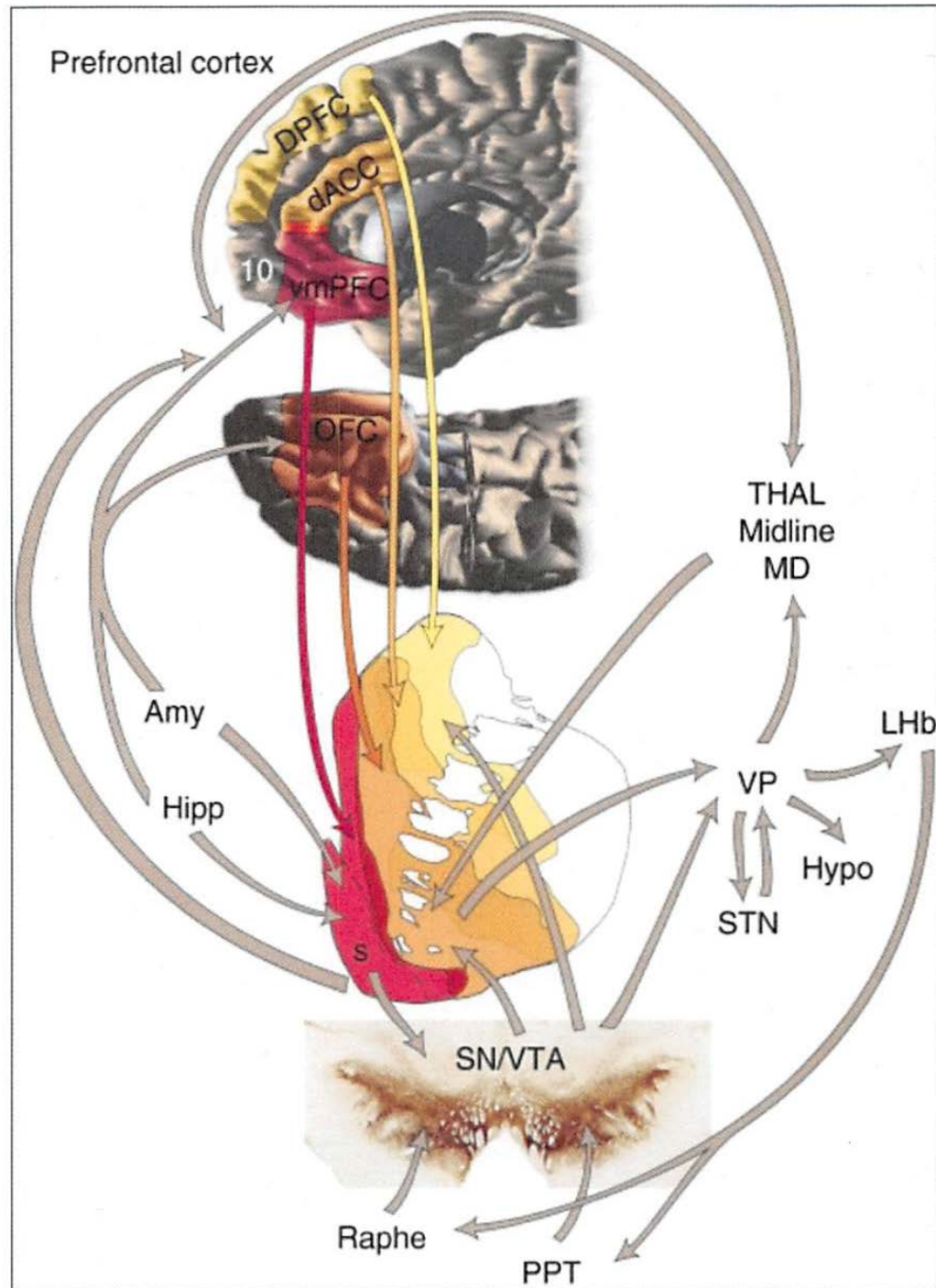
- One learns that some action is likely to lead to a reward.
- Likelihood of doing the action is sensitive to the reward value of the outcome.
- Critical to acquisition of new behaviors.
- Key neural substrates:
  - Amygdala
  - Ventral striatum (NAc)
  - Orbitofrontal cortex

Rolls (2005): pp. 152-5,185;  
Graybiel (2008)  
Shohamy (2011)

# Stimulus-Response Learning (Habit Formation)

- Behavior becomes insensitive to reward value of the outcome.
- Key neural substrates:
  - Dorsolateral striatum (caudate/putamen)
  - Dorsolateral prefrontal cortex

Graybiel (2008)  
Balleine & O'Doherty (2011)



Haber & Knutson,  
(2010)

# Characteristics of Habits

(Graybiel, 2008)

## Habits:

- Are learned behaviors (not innate)
- Occur repeatedly and become fixed (“overtraining”)
- Once acquired, occur automatically, almost unconsciously
- Involve a structured behavioral sequence prone to be elicited by a particular context or stimulus



# London



# Is Dieting in Anorexia Nervosa Habitual?

- Is learned behavior (not innate):
  - Dieting is clearly learned.
- Occurs repeatedly and become fixed:
  - Repetition required to lose weight.
- Once acquired, occurs automatically, almost unconsciously:
  - No clear data, but dieting behavior occurs despite conscious desire to eat more normally.
- Involves a structured behavioral sequence prone to be elicited by a particular context or stimulus:
  - Eating behavior often involves rituals.
  - Meals, and a range of other stimuli, including negative emotion, may constitute a sufficient stimulus.



# Hypothesis

The eating behaviors characteristic of individuals with Anorexia Nervosa begin as goal-directed (A-O learning) but become habitual.

And, therefore, highly resistant to change.

And, thereby, serve to perpetuate the disorder.

# ***How does dieting/exercise become habitual?***

- Initially (at least), it is rewarding.
  - Therefore, supports action-outcome learning.
  - Reward is intermittent and behaviors are repeated and become “over-trained.”
- Occurs during adolescence.
  - A time of bias towards reward (vs adverse outcomes).
  - A time of multiple stresses.
- Enhanced by starvation.



Preliminary, unpublished, data not shown.

# Thank you!

More information:

<http://columbiaeatingdisorders.org/>

(including T32 post-doctoral program on  
Research on Eating Disorders)