

# **OCD & Anxiety Lecture Series**

## **Register today on Ethos**

All dates: 9:00 am – 12:15 pm

### **Sessions I & II - Friday, March 26, 2021**

**Session I:** Core Concepts in Diagnosing and Treating Obsessive Compulsive Disorder with Cognitive Behavioral Therapy - Jon Hershfield, MFT

**Session II:** Medication Protocols for Obsessive Compulsive Disorder, New Research, and Differential Diagnosis - Robert Hudak, MD

### **Sessions III & IV - Friday, April 23, 2021**

**Session III:** Treating Pediatric Obsessive Compulsive - Aureen Pinto Wagner, PhD

**Session IV:** Working With Families and Treatment Refusal - C. Alec Pollard, PhD

### **Sessions V & VI - Friday, May 21, 2021**

**Session V:** Inhibitory Learning Theory in Exposure-based Treatment of Obsessive Compulsive Disorder - Jonathan Abramowitz, PhD

**Session VI:** Disgust and Not Just Right Experiences in Obsessive Compulsive Disorder - Dean McKay, PhD

# Psychology Workshops

## Register today on Ethos

All dates: 9:00 am – 12:15 pm

**Friday, March 12, 2021, 9:00 am – 12:15 pm, Virtual Classroom**

*Evidence Based Care for Refugee, Asylee, and Immigrant Patients*

Rachel R. Singer, PhD and Renee DeBoard-Lucas, PhD

**Friday, May 7, 2021, 9:00 am - 12:15 pm, Virtual Classroom**

*A Workshop on Motivational interviewing: Gaining Traction with Patients Who Feel Stuck*

Rachel Smolowitz, PhD

**Friday, June 5, 2021, 9:00 am – 12:15 pm, Virtual Classroom**

*Clinical Suicidology: Innovations in the Assessment and Treatment of Suicidal Risk*

David Jobes, PhD, ABPP

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**Steven A. Rasmussen, MD**, reports as having no financial interest, arrangement or affiliation with *any entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on, patients*, during the past 12 months. He will discuss Medtronic, an Irish device company, in this presentation.

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# Learning Objectives

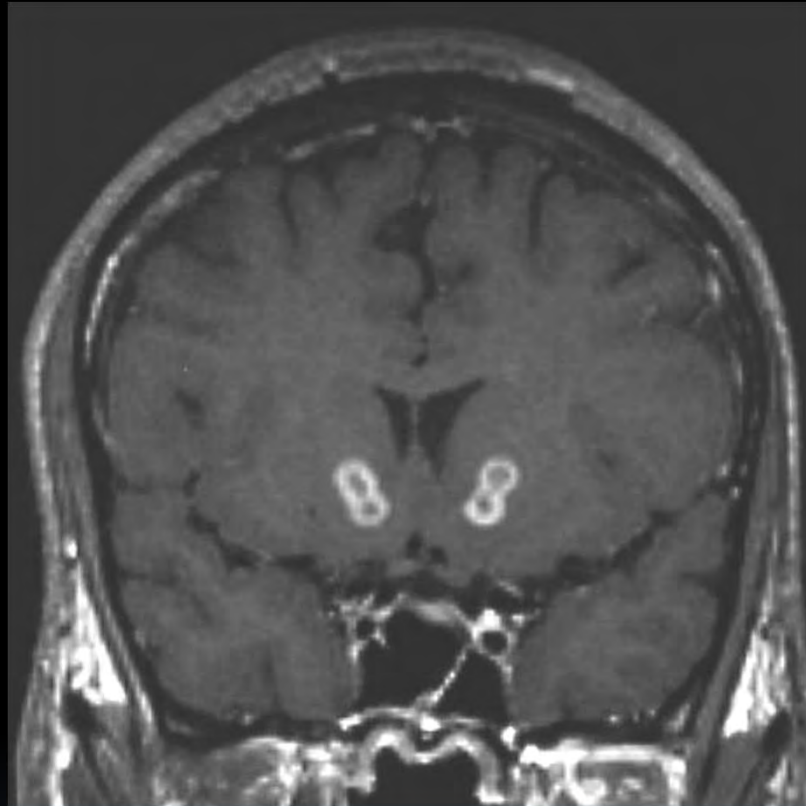
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**After attending this program, participants will be able to:**

1. Identify the two major core features of Obsessive Compulsive Disorder.
2. Compare the effectiveness of exposure based versus pharmacologic treatments for Obsessive Compulsive Disorder.
3. Discuss neurosurgical approaches to the treatment of intractable Obsessive Compulsive Disorder.

# OCD: A Generation of Progress

Sheppard Pratt Hospital  
January 2021



Jane Eisen, M.D.  
Ben Greenberg, M.D. Ph.D  
Maria Mancebo, Ph.D  
Richard Marsland, R.N.  
Georg Noren, M.D. Ph.D  
Steve Rasmussen, M.D.



# **A Half Century's Stasis**

**Antipsychotic drugs: Efficacy peaked in early 1960s (clozapine); 2nd generation no more efficacious than 1st for schizophrenia**

**Antidepressants: Efficacy plateaued in 1957—all real advances in safety and tolerability (e.g., SSRIs)**

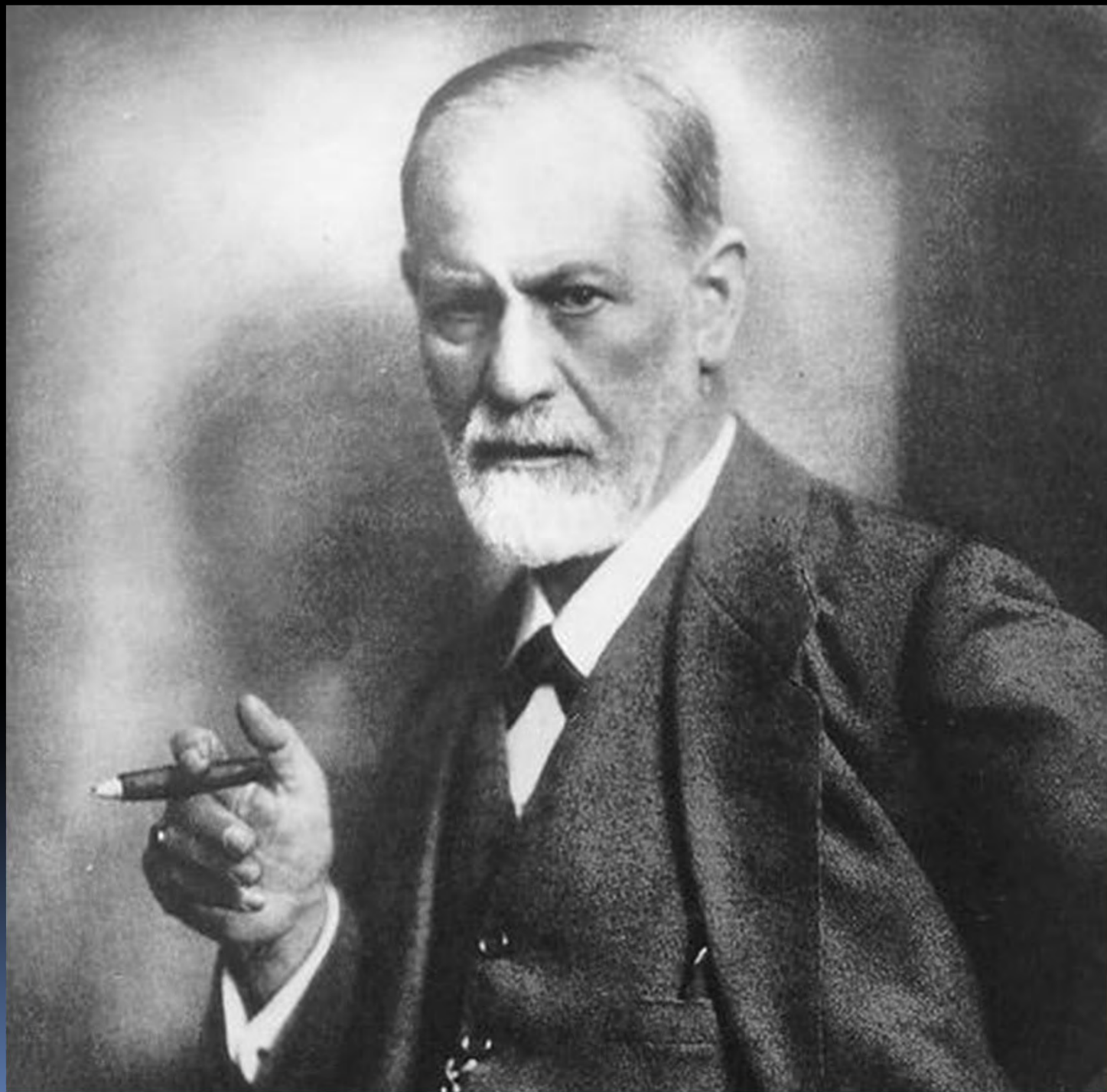
**Lithium (1949) still necessary despite severe side effects**

**No drug Rx for core autism symptoms, cognitive symptoms of schizophrenia; Rx poor for bipolar depression**



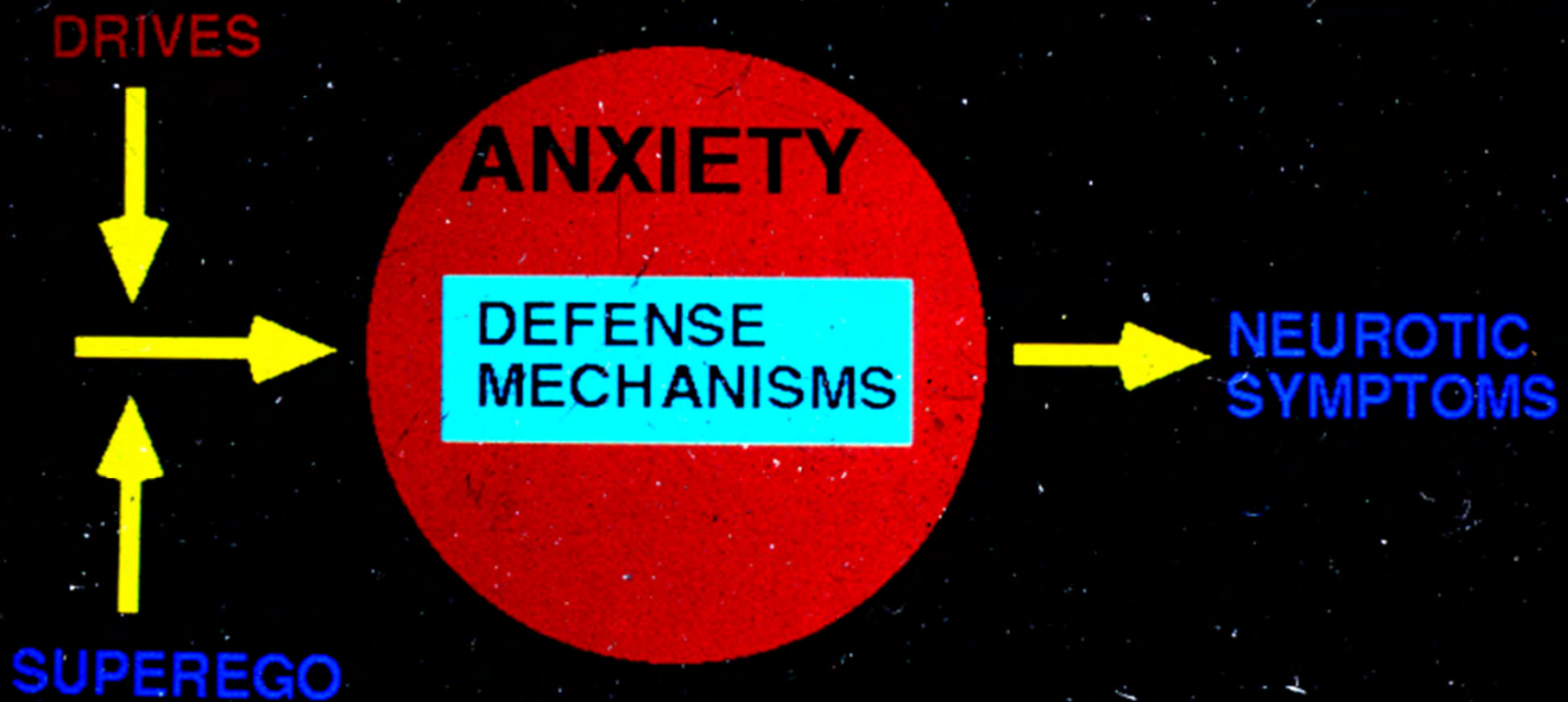
*Lady Macbeth. - Yet here's a spot.  
Doctor. - Hark! she speaks.  
Act V. Scene I.*





# FORMATION OF NEUROTIC SYMPTOMS

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# LIFETIME PREVALENCE OF OCD



# **OCD: Crippling Obsessions & Checking**

## **OC SYMPTOMS ON ADMISSION** (N=250)

<b><u>Obsessions</u></b>	<b>%</b>	<b><u>Compulsions</u></b>	<b>%</b>
<b>Contamination</b>	<b>45</b>	<b>Checking</b>	<b>63</b>
<b>Pathological doubt</b>	<b>42</b>	<b>Washing</b>	<b>50</b>
<b>Somatic</b>	<b>36</b>	<b>Counting</b>	<b>36</b>
<b>Need for symmetry</b>	<b>31</b>	<b>Need to ask or confess</b>	<b>31</b>
<b>Aggressive</b>	<b>28</b>	<b>Symmetry and precision</b>	<b>28</b>
<b>Sexual</b>	<b>26</b>	<b>Hoarding</b>	<b>18</b>
<b>Other</b>	<b>13</b>	<b>Multiple compulsions</b>	<b>48</b>

Rasmussen and Eisen, 1988

## Yale-Brown Obsessive Compulsive Scale (YBOCS)

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- Obsessions and compulsions are evaluated in analogous fashion with respect to how much they:
  - occupy the person's time
  - interfere with function
  - cause subjective distress
  - are resisted
  - can actually be controlled



# SRI Drug Response at 16 Weeks in OCD

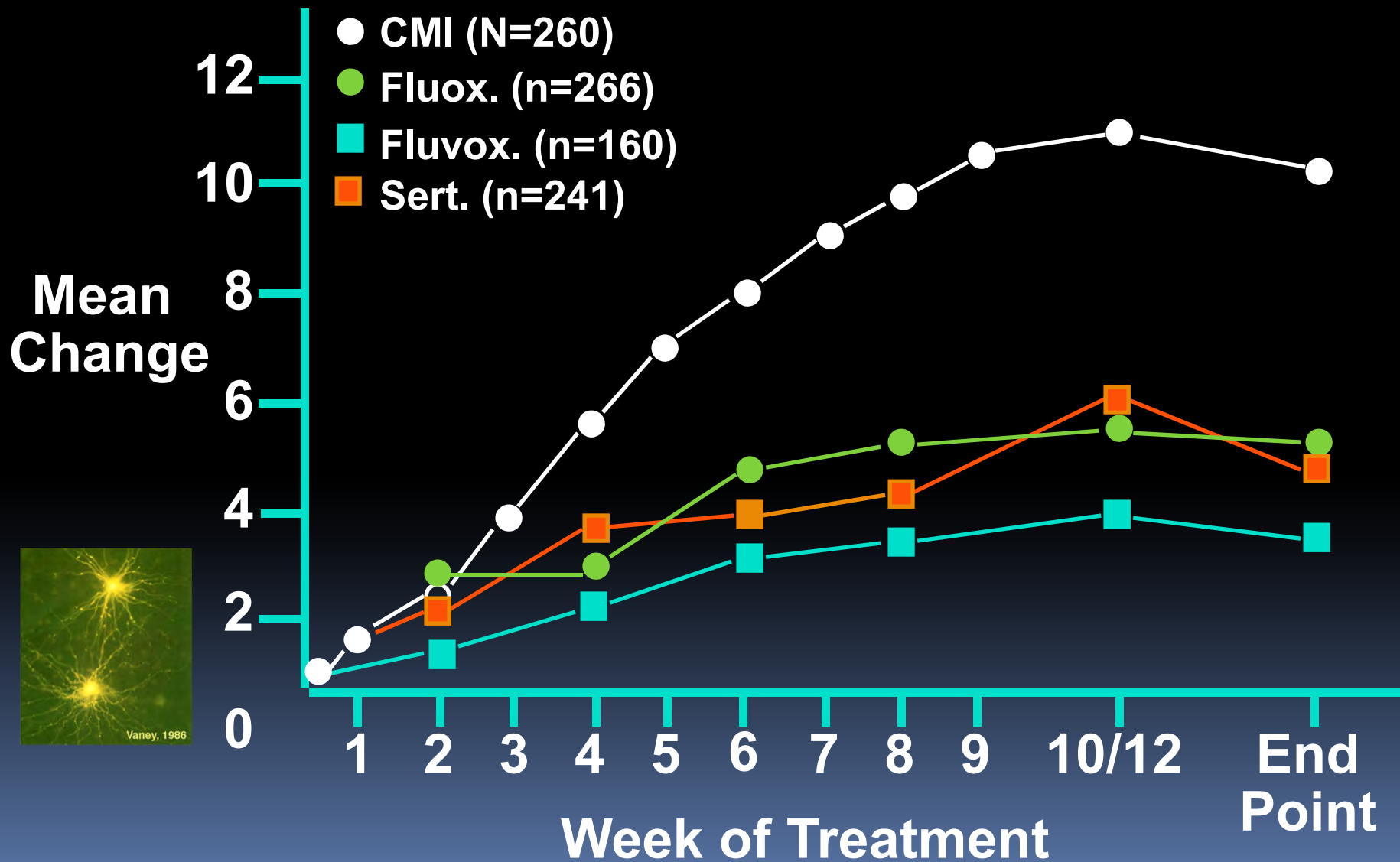
**(CMI=68)**

**(FLV=27)**

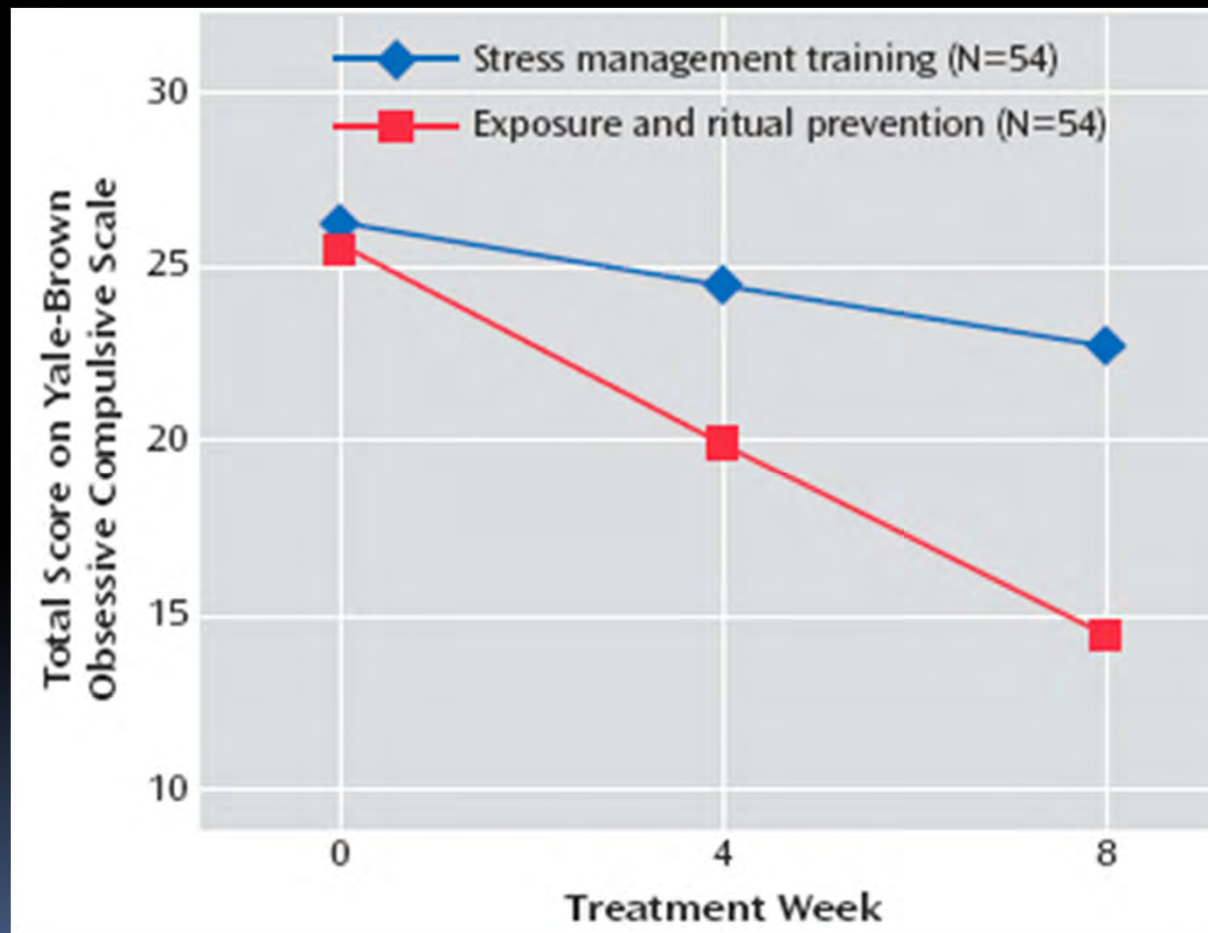
**(FLX=43)**

<b>Very much improved</b>	<b>8%</b>
<b>Much improved</b>	<b>22%</b>
<b>Moderately improved</b>	<b>41%</b>
<b>Minimally improved</b>	<b>17%</b>
<b>Not improved</b>	<b>12%</b>

# Mean changes in total YBOCS scores for drug intent-to-treat analysis



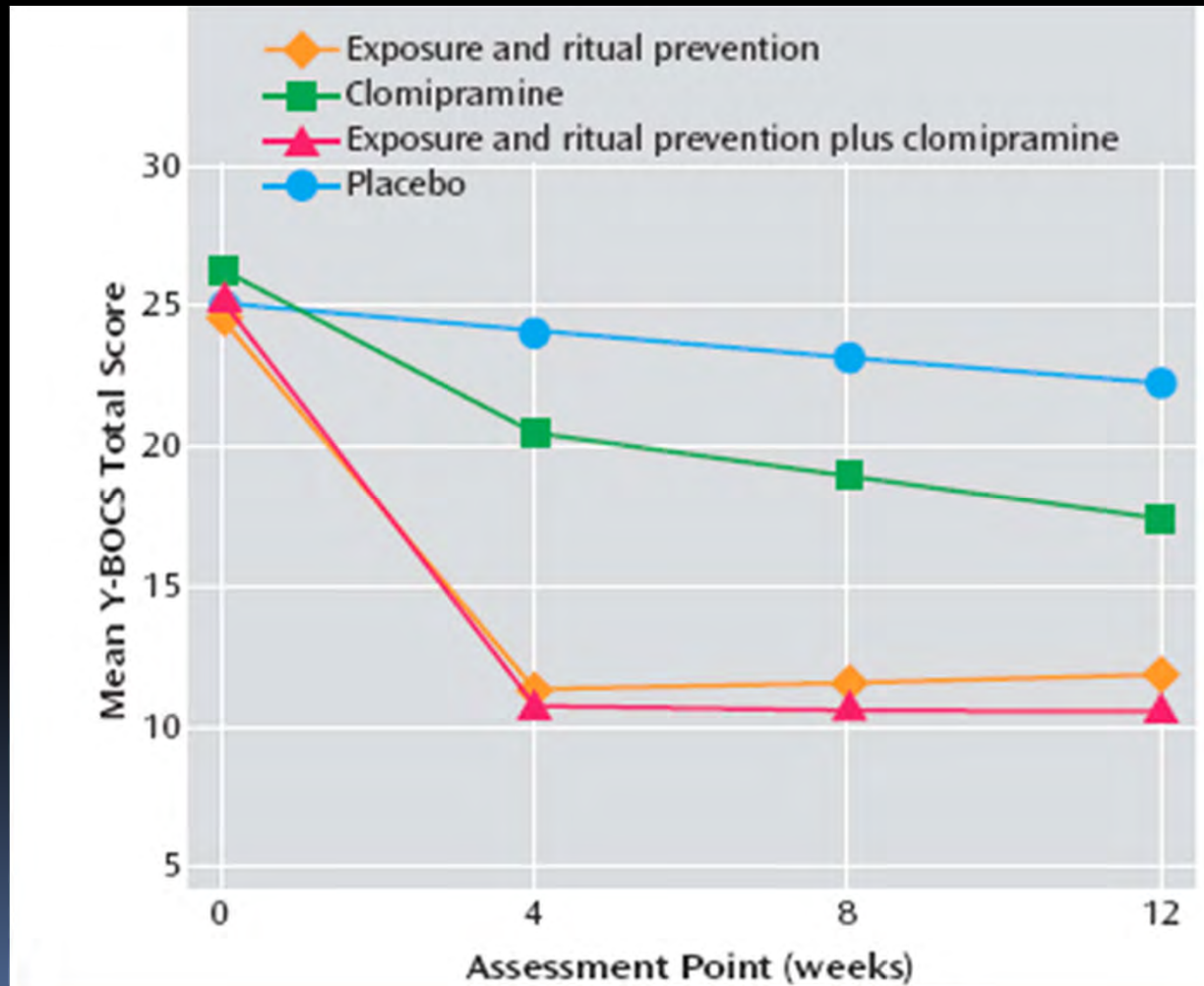
# CBT Augmentation of SRI



17 90-120 minute sessions

Simpson et al 2008

# SRIs versus ERP



# Treatments for OCD

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## Treatment

## Response Rate

**SRI**

**60-70%**

**CBT**

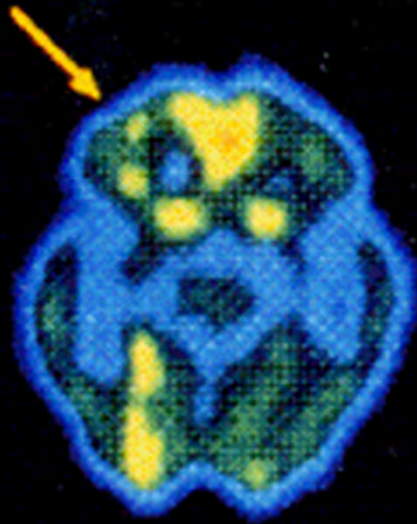
**70-80%**

**SRI & CBT**

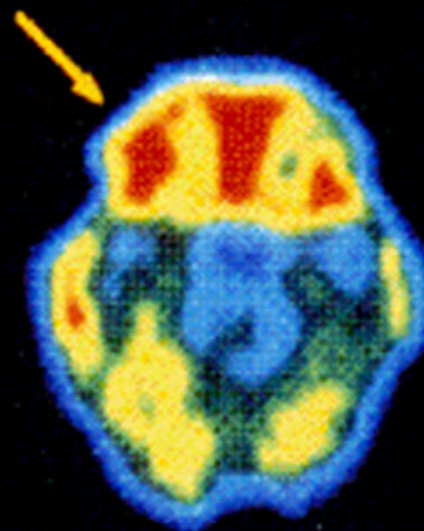
**80-85%**

# OCD: Resting FDG-PET

High Orbital Glucose Metabolism



Normal  
Control

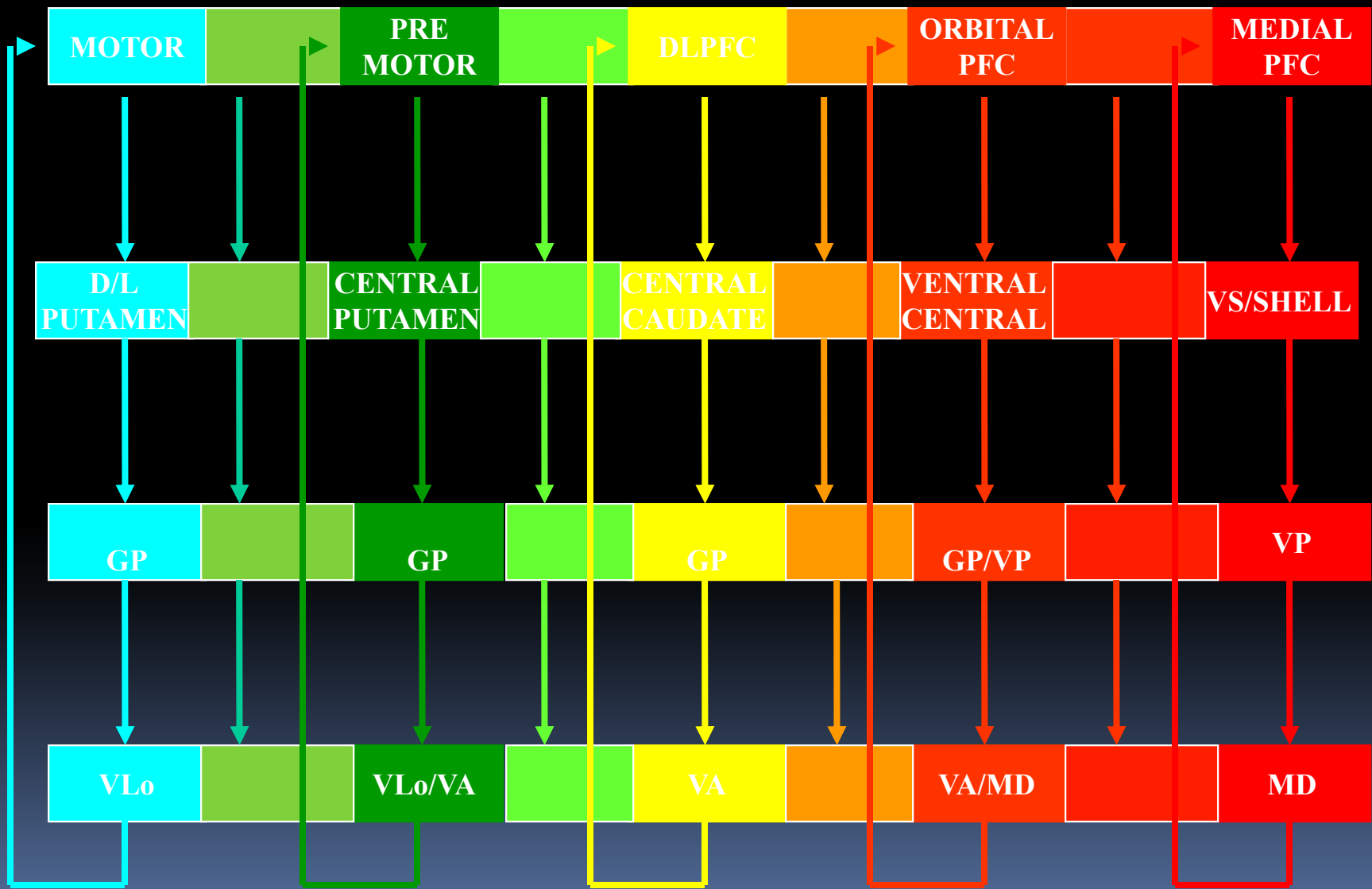


Obsessive  
Compulsive

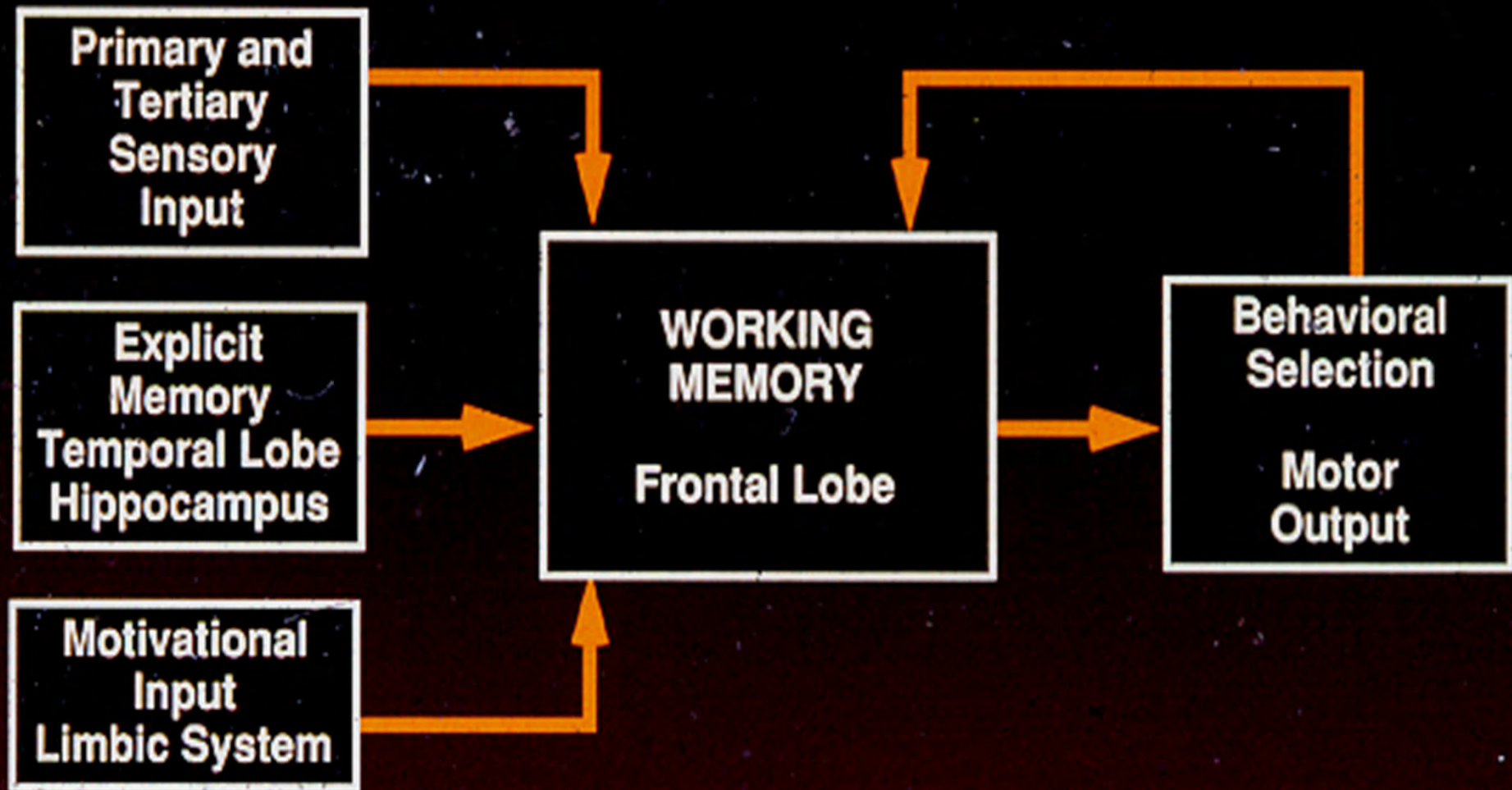
54.3  
52.0  
49.6  
47.2  
44.9  
42.5  
40.2  
37.8  
35.4  
33.1  
30.7  
28.3  
26.0  
23.6  
21.3  
18.9  
16.5  
14.2  
11.8  
9.5  
7.1  
4.7  
2.4  
0.0

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# FUNCTIONAL TOPOGRAPHY OF CORTICO-BG PATHWAYS



# AUTOMATIC PROCESSING AND THE FRONTAL LOBE





# OCD Core Features

**HARM AVOIDANCE**  **INCOMPLETENESS**

**Anxiety Disorders**

**Tics OCPD Hoarding**

**Behavioral Inhibition**

**Anakastic Traits**

**Fear Potentiated Startle  
Avoidance Devaluation  
Extinction Recall**

**Planning  
Task Switching  
Delay Discounting**

**Amygdalofrontal  
Salience Network**

**FP SMA IFG  
Cognitive Control Network**

# **Intractable OCD**

**Failed trials of 3-5 SRIs including CMI**

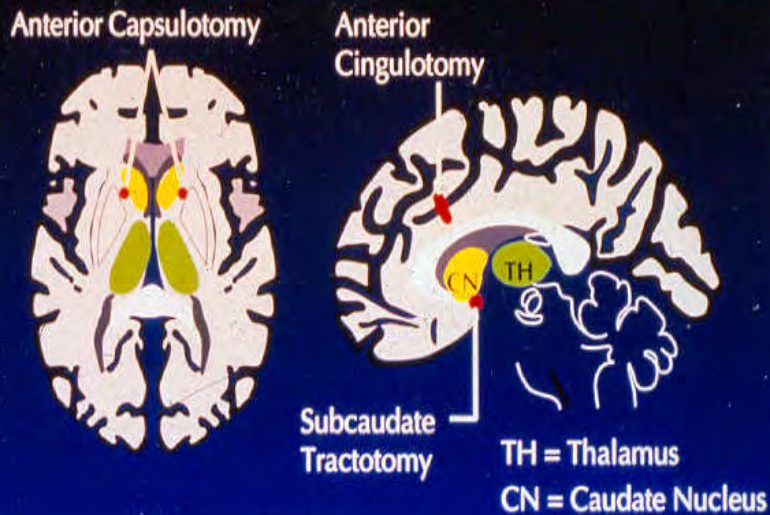
**Failed adequate trial of CBT in combination with SRI**

**Failed augmentation with neuroleptic BZD Buspar**

**Severe deteriorative course of illness**

# Neurosurgical Procedures for OCD

## Neurosurgery in OCD

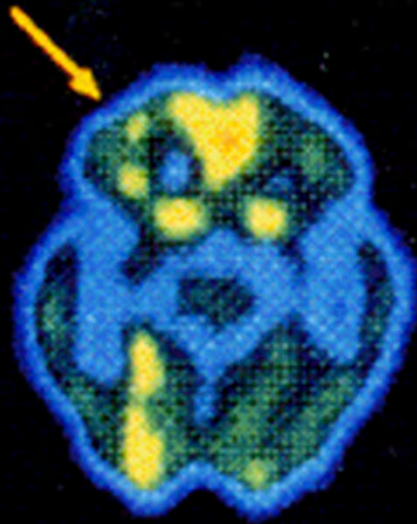


## Symptom Free or VMI

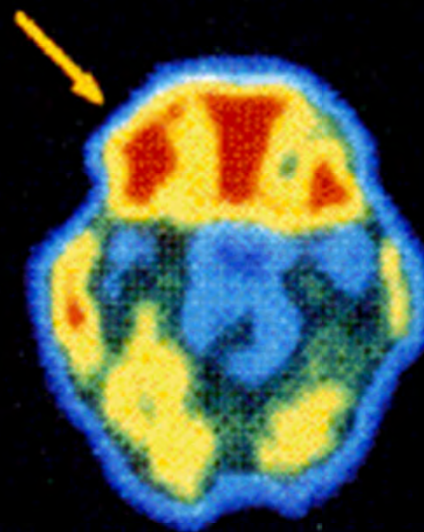
- |                           |     |
|---------------------------|-----|
| 1. Capsulotomy            | 67% |
| 2. Cingulotomy            | 56% |
| 3. Subcaudate Tractotomy  | 50% |
| 4. Limbic Leucotomy (2+3) | 61% |

# OCD: Resting FDG-PET

High Orbital Glucose Metabolism



Normal  
Control



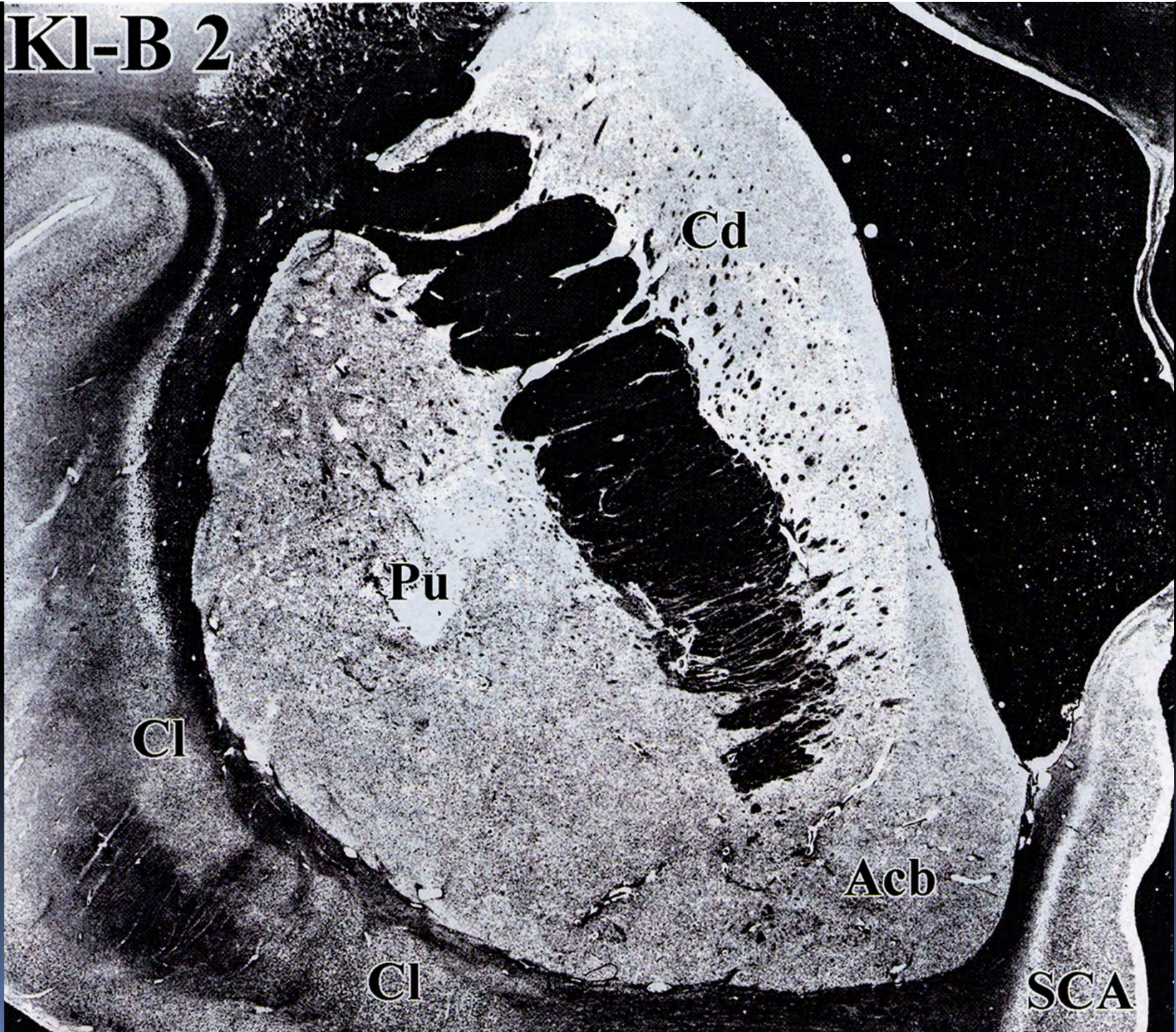
Obsessive  
Compulsive

54.3  
52.0  
49.6  
47.2  
44.9  
42.5  
40.2  
37.8  
35.4  
33.1  
30.7  
28.3  
26.0  
23.6  
21.3  
18.9  
16.5  
14.2  
11.8  
9.5  
7.1  
4.7  
2.4  
0.0

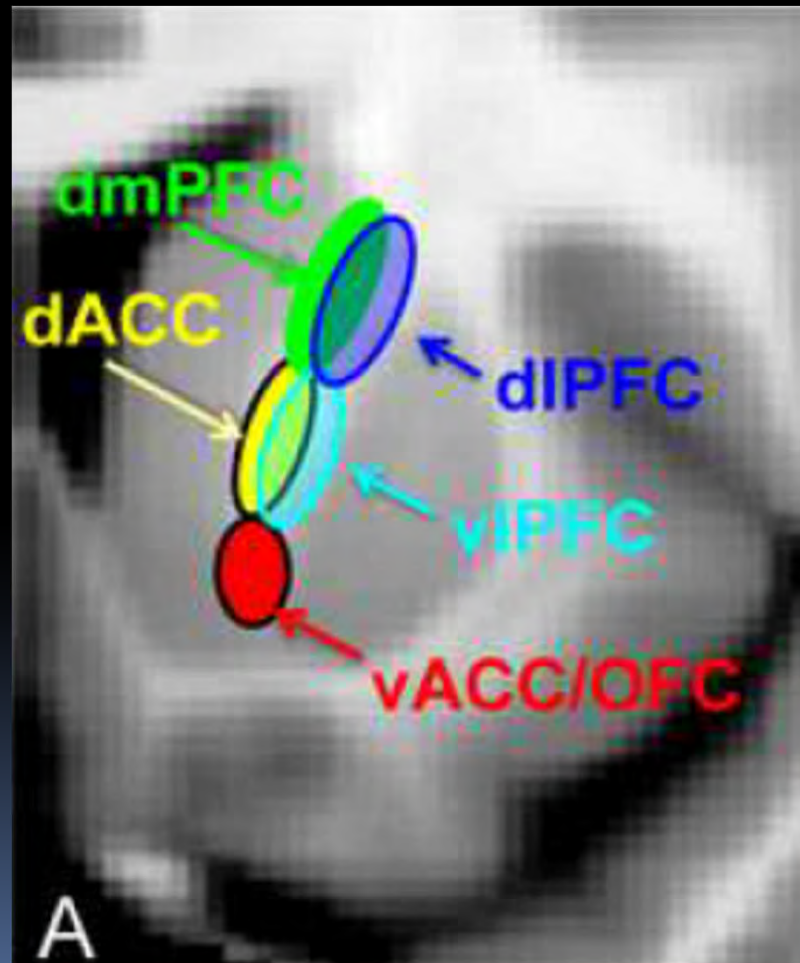
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**KI-B 2**



# Corticofugal fibers in ALIC



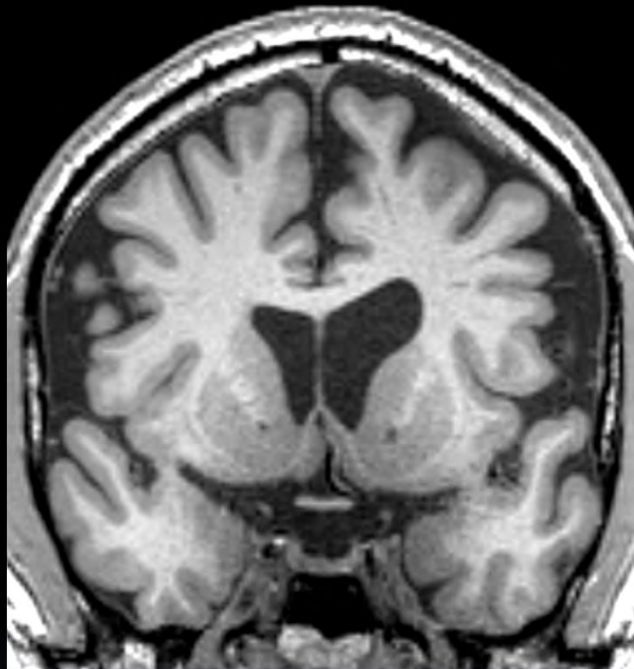
# **Gamma Capsulotomy for OCD**

- Hypothesis driven treatment based on imaging findings
- Targeted OFC and MPFC connections with midline thalamic nuclei and brainstem
- Lesion in internal capsule 8-10 mm rostral to posterior border of anterior commissure
- 55 treatment intractable pts with OCD 1993-2010
- 15 of 55 with a two stage lesion

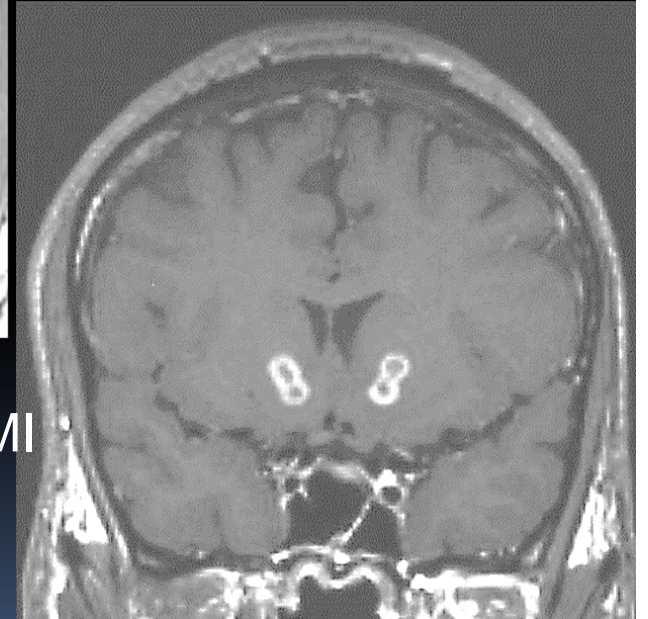




Single Shot n=15 7%VMI



Single shot n=11 0% VMI



Double Shot n=55 55%VMI

# Before Gamma Capsulotomy

(4 "shots" eventually made)



## Gamma Ventral Capsulotomy: YBOCS Responder Rates, Staged and Combined Cohorts



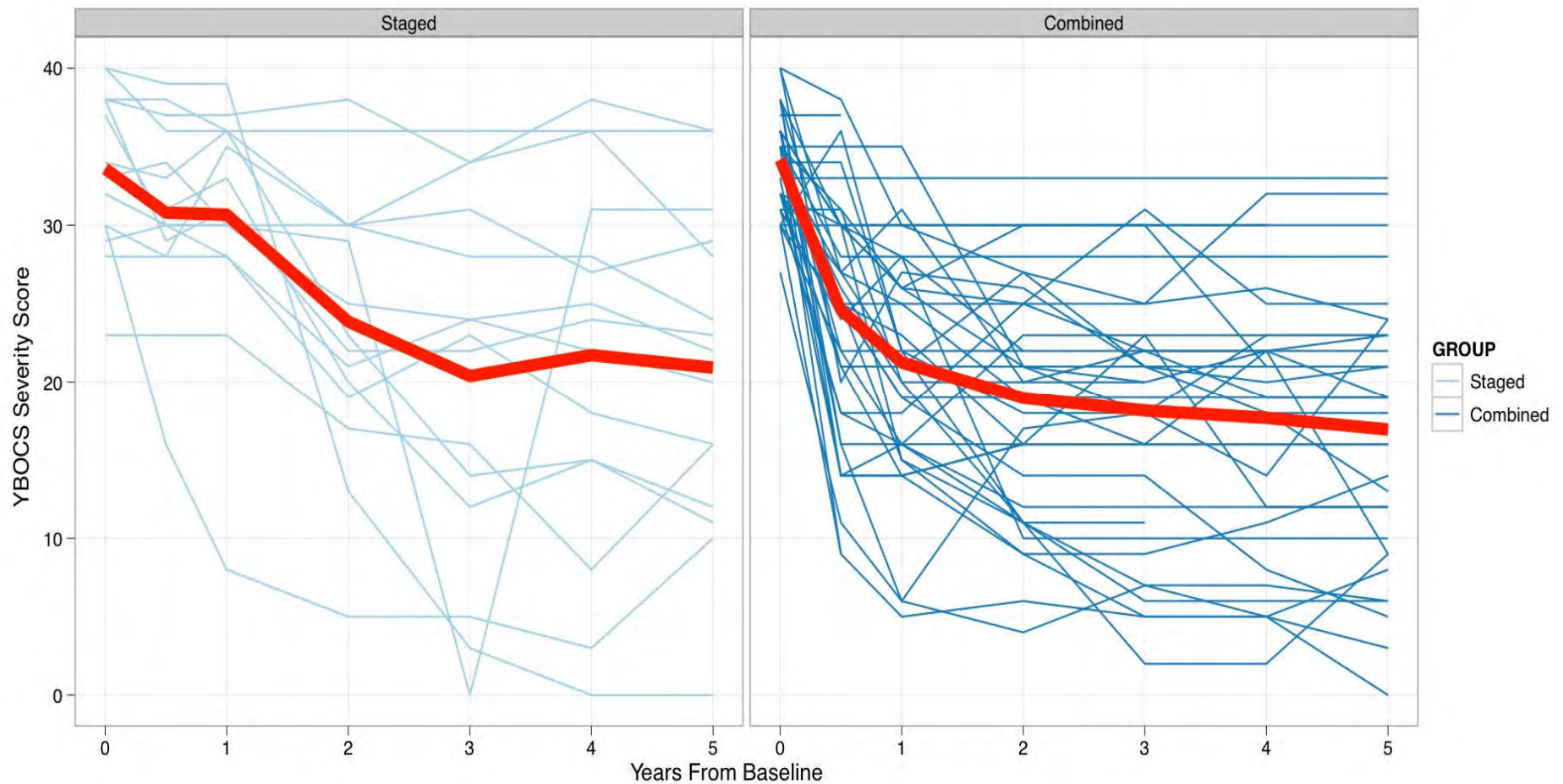
<b>Time since surgery</b>	<b>&lt;25%</b>	<b>25-34%</b>	<b>35% +</b>	<b>Total</b>
<b>Staged Group*</b>				
6 months	11 (73%)	1 (7%)	3 (20%)	15
1 year	8 (53%)	2 (13%)	5 (33%)	15
2 year	7 (47%)	3 (20%)	5 (33%)	15
3 year	7 (47%)	1 (7%)	7 (47%)	15
4 year	7 (47%)	1 (7%)	7 (47%)	15
5 year	5 (33%)	4 (27%)	6 (40%)	15
<b>Combined Group</b>				
6 months	21 (53%)	6 (15%)	13 (33%)	40
1 year	11 (29%)	7 (18%)	20 (53%)	38
2 year	9 (27%)	5 (13%)	24 (63%)	38
3 year	8 (22%)	3 (8%)	26 (70%)	37
4 year	6 (17%)	8 (23%)	21 (60%)	35
5 year	5 (16%)	5 (16%)	22 (69%)	32

\* Staged group time points are indicated from the second surgery, percent changes in ratings are vs the original baseline.

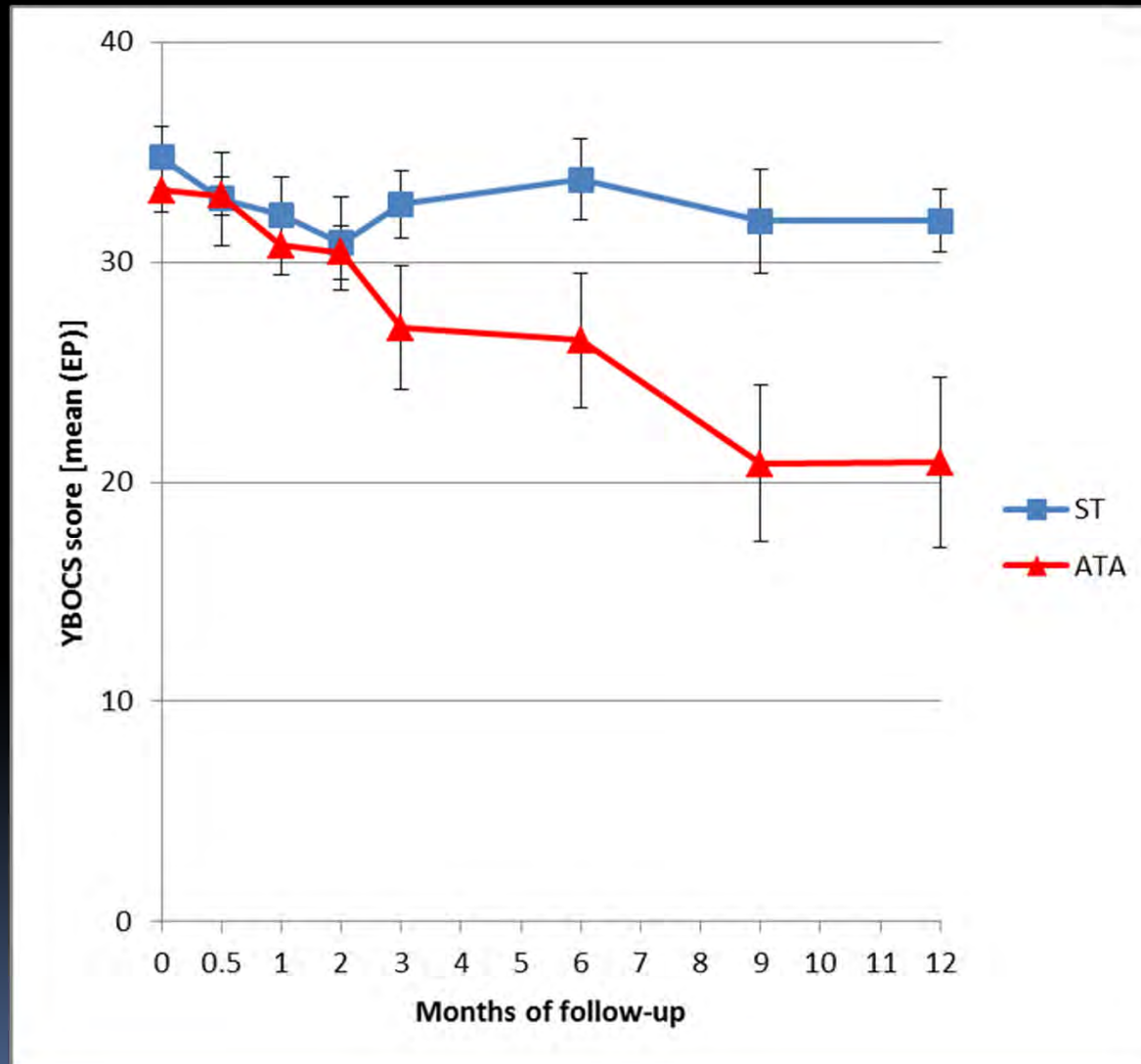
### Gamma Ventral Capsulotomy Outcomes

Group	Baseline	6 mo.	1 yr.	2 yr.	3 yr.	4 yr.	5 yr.
<b>Staged (n=15)</b>							
YBOCS (M ± s)	33.6 ± 5.0	29.3 ± 6.6	26.8 ± 6.9	23.9 ± 8.7	20.4 ± 11.7	21.7 ± 11.8	20.9 ± 10.3
HAM-D (M ± s)	24.3 ± 8.7	23.4 ± 6.4	21.9 ± 9.2	22.7 ± 12.7	18.4 ± 13.5	20.2 ± 14.3	19.8 ± 12.0
HARS (M ± s)	19.3 ± 8.5	15.4 ± 3.9	15.9 ± 4.3	16.6 ± 10.6	14.1 ± 11.4	15.9 ± 10.7	14.3 ± 11.0
GAF (M ± s)	33.7 ± 7.9	35.5 ± 8.3	41.4 ± 8.6	44.3 ± 10.8	48.7 ± 15.6	50.4 ± 16.7	52.7 ± 13.8
<b>Combined (n=40)</b>							
YBOCS (M ± s)	34.2 ± 3.2	24.6 ± 7.7	21.3 ± 7.4	19.0 ± 7.4	18.2 ± 8.2	17.7 ± 8.4	16.8 ± 8.6
HAM-D (M ± s)	27.7 ± 9.7	23.0 ± 10.1	20.1 ± 9.5	16.8 ± 8.6	16.1 ± 8.9	16.0 ± 9.5	15.2 ± 9.6
HARS (M ± s)	20.0 ± 9.4	15.6 ± 9.4	14.0 ± 7.9	12.1 ± 5.8	12.1 ± 6.4	11.1 ± 6.6	10.8 ± 6.2
GAF (M ± s)	38.8 ± 6.9	46.3 ± 7.7	50.5 ± 9.1	54.7 ± 11.4	56.2 ± 12.2	58.2 ± 12.7	60.3 ± 14.5

# YBOCS after Staged or Combined Gamma Ventral Capsulotomy



# Brazilian Double Blind OCD Study



# GVC for Intractable OCD: Efficacy

**TABLE 3. Literature review of patients with OCD who underwent GKRS for anterior capsulotomy**

Authors & Year	No. of Pts	Mean Age (yrs)	Mean FU (mos)	Max Dose, Gy (shots)	Mean Y-BOCS Score		Responders (%)
					Before GKRS	After GKRS	
Rück et al., 2008	9	43.9	136.8	180–200 (1–3)	33.4	14.2	5 (56)
Lopes et al., 2004	5	35	48	180 (2)	32	24	3 (60)
Gouvea et al., 2010	1	34	12	180 (2)	37	0	—
Kondziolka et al., 2011	3	44	42	140–150 (2)	37.3	16.3	2 (67)
Sheehan et al., 2013		38	26	140–160 (1)	32	17	4 (80)
Lopes et al., 2014–2015	12	33.9	55.2	180 (2)	33.6	17.3	7 (58.3)
Present series	10	41.2	41	120 (2)	32.7	14.7	7 (70)

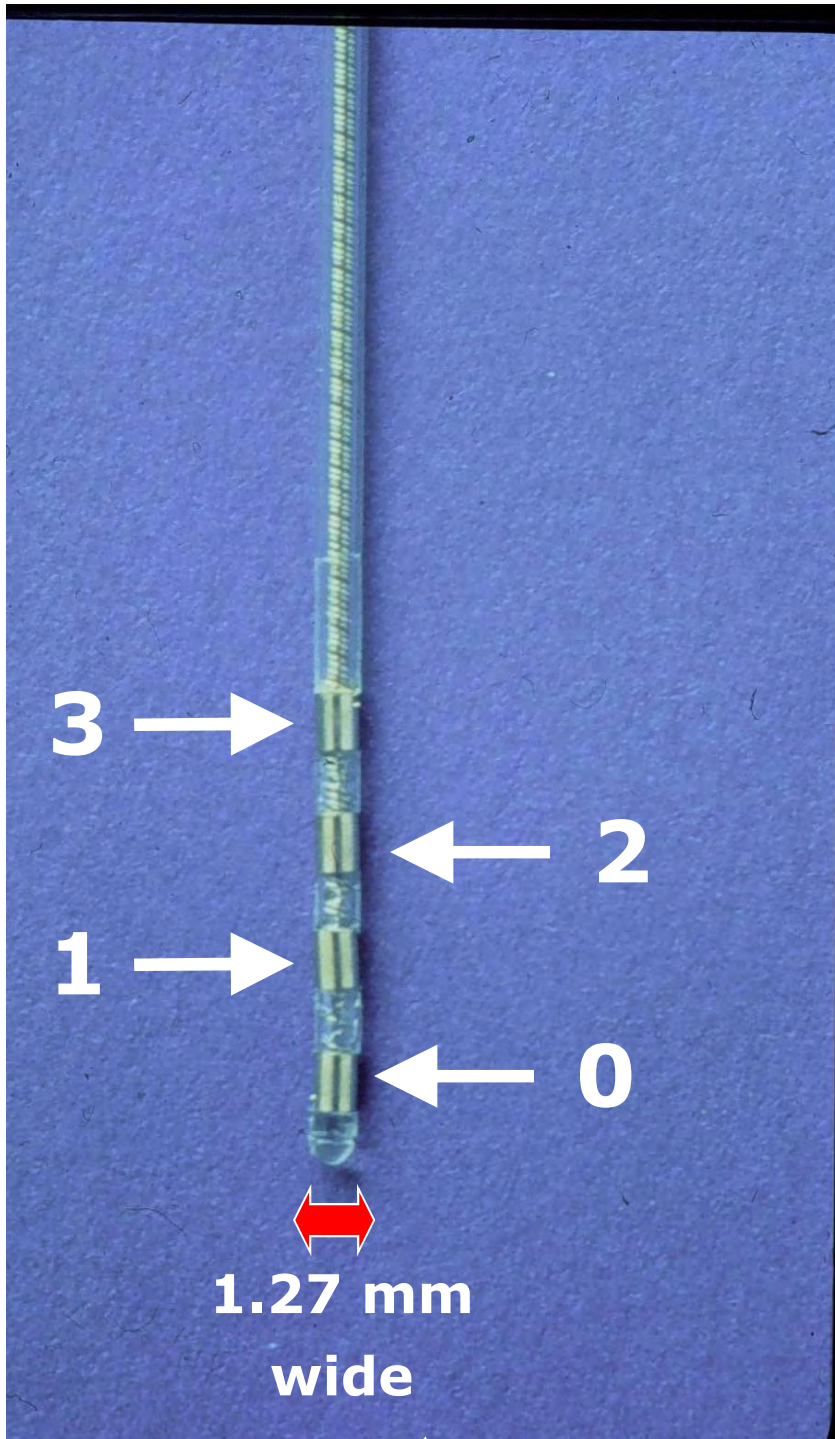
## **Gamma Capsulotomy Double Shot: Adverse Events**

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- **No neuropsychological deficits**
- **1/40 apathy & amotivation**
- **9/40 edema & headache (steroid Tx in 6)**
- **3/40 asymptomatic caudate infarction**
- **2/40 possible exacerbation of MDI**
- **3/40 late developing cysts**







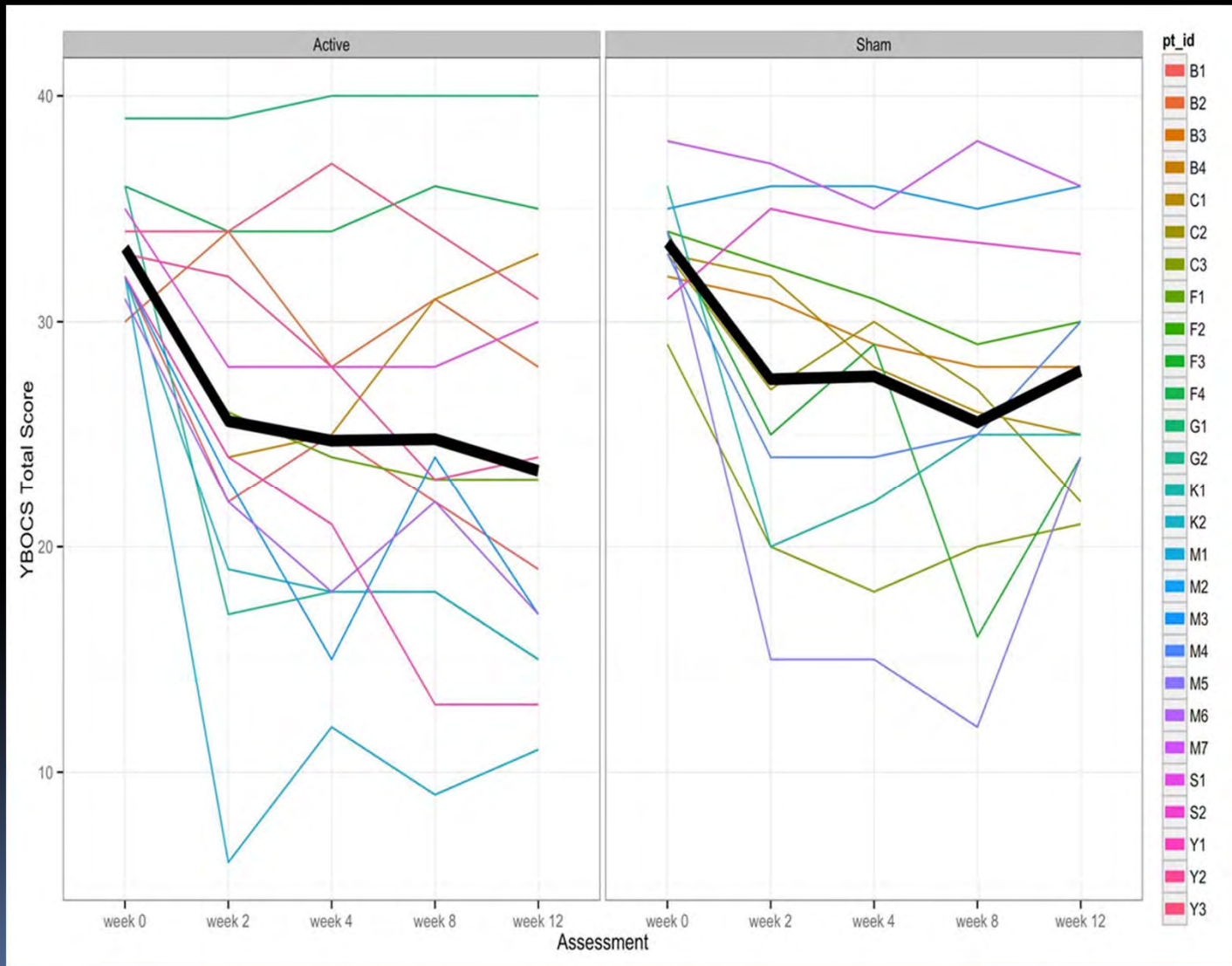
**4 electrodes  
on each brain lead,  
numbered 0-3,  
ventral to dorsal**



**IPG**



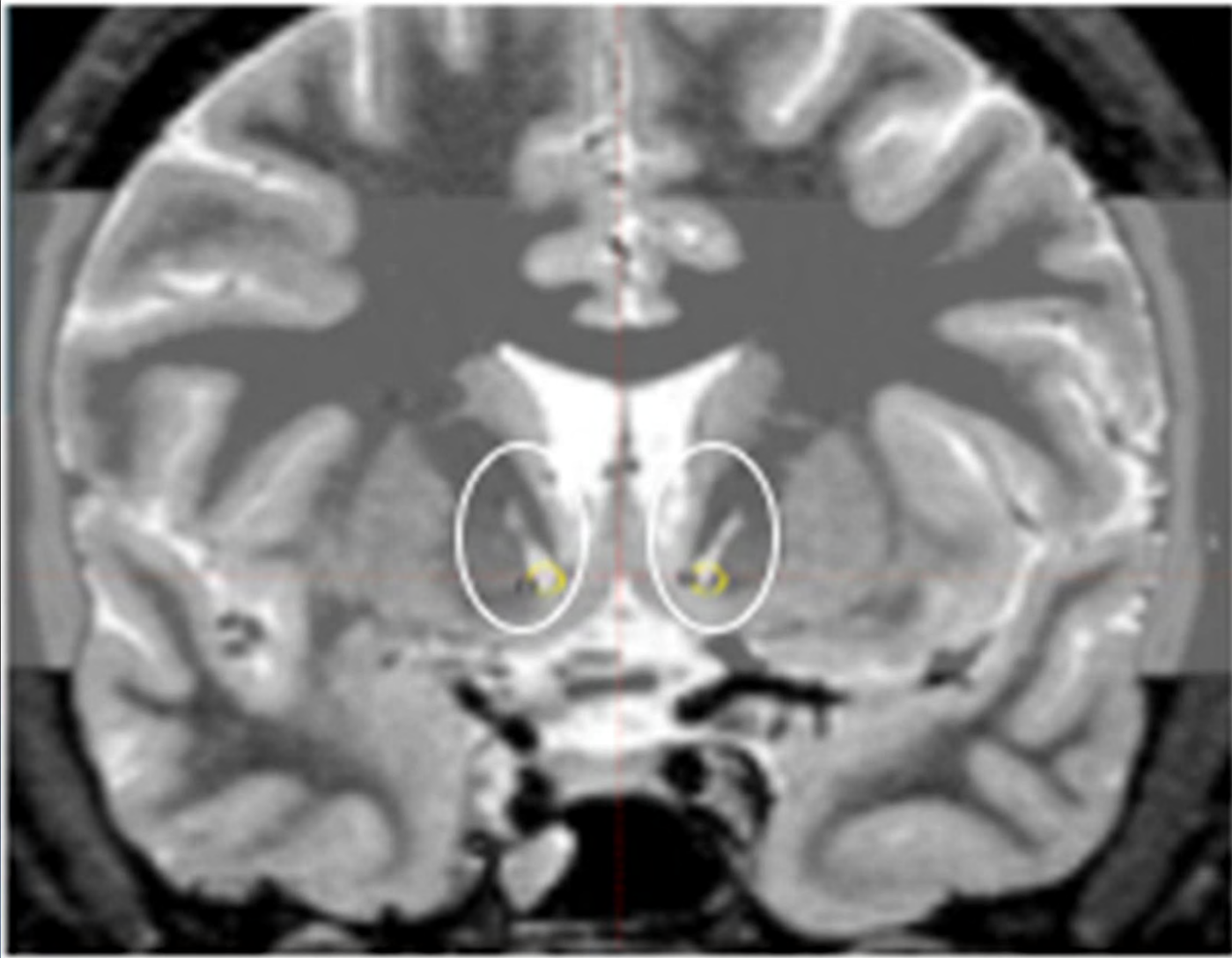
# YBOCS scores DBS NIMH Trial (n=27)



# Leuven 1<sup>st</sup> VC/VS DBS implant Nuttin et al

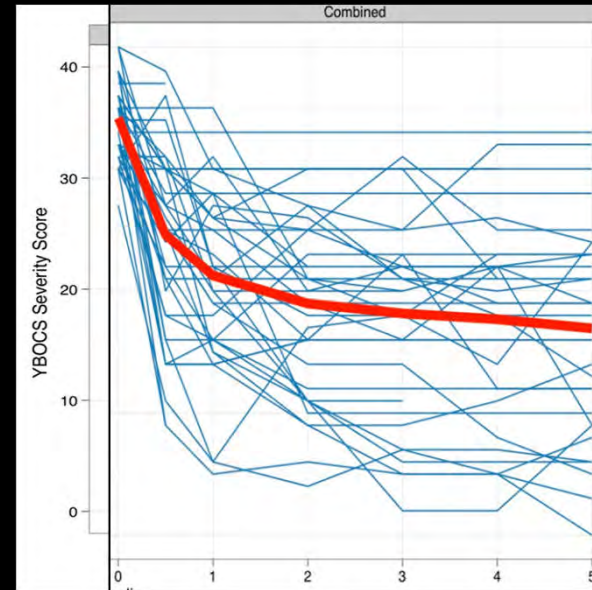
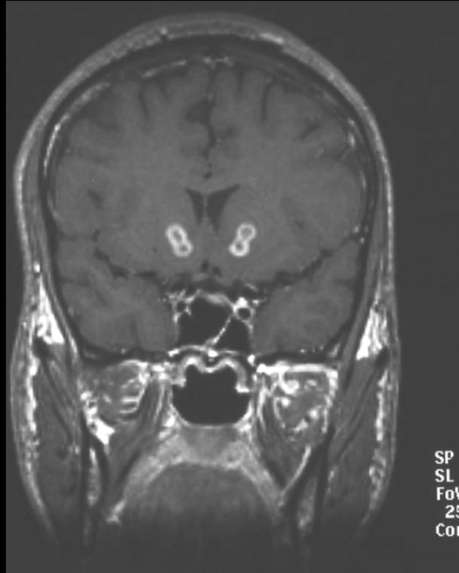


# vALIC DBS for OCD

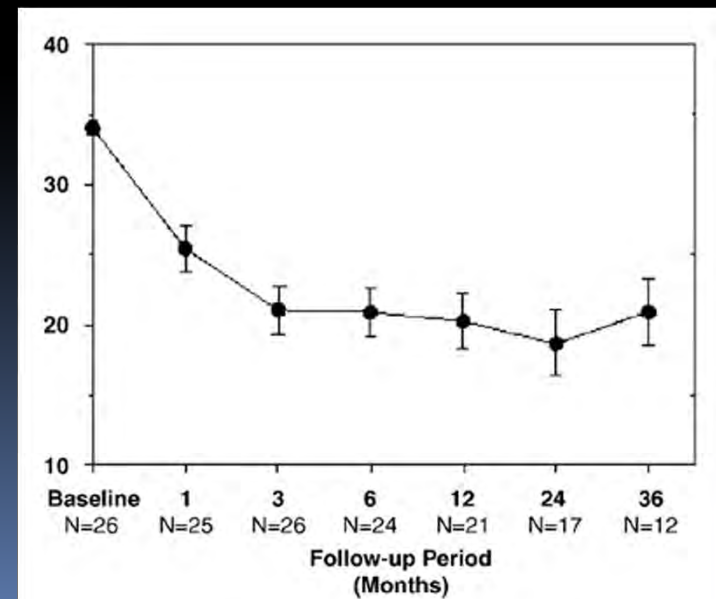
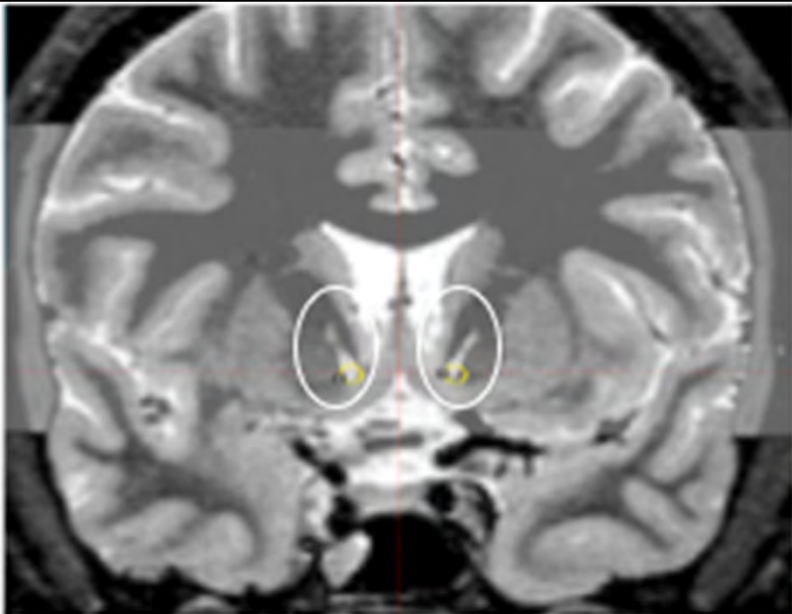




# Gamma Knife Outcomes in OCD



# DBS Outcomes in OCD

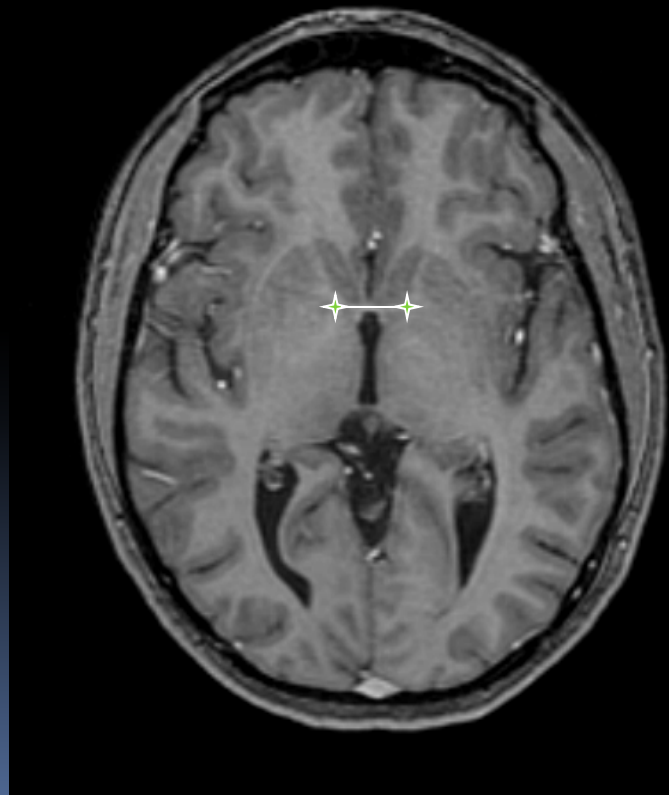




# DBS for OCD NIMH Trial

- Original Electrode
  - Medtronic 3391
  - 3 mm contacts
  - 4 mm spacing
- Controlled Trial
  - Model 3387
  - 1.5 mm contacts
  - 1.5 mm spacing
- Activa PC (blinded phase)
- Activa RC (rechargeable, open phase)

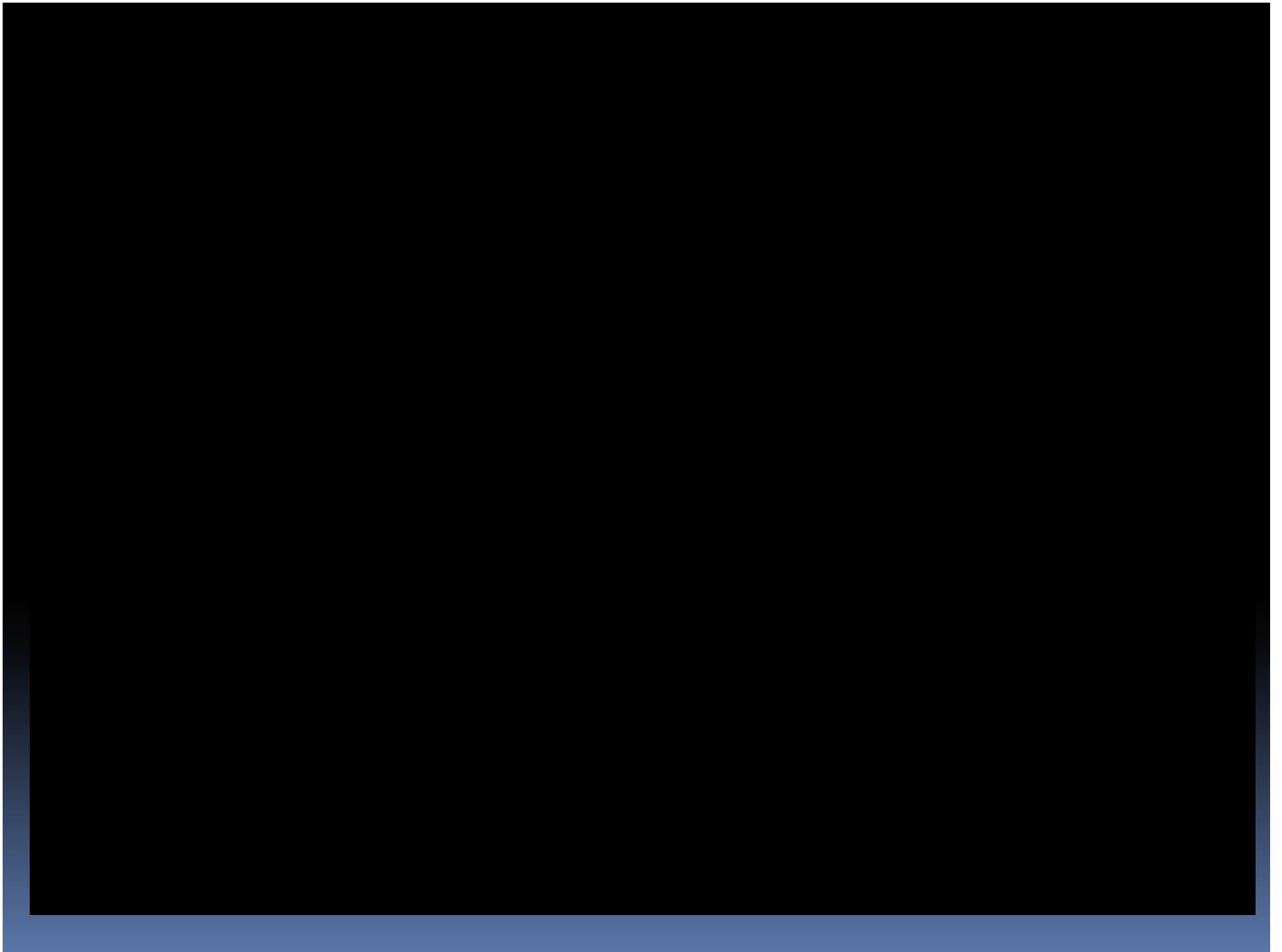
DBS extent model 3387



Courtesy E. Eskandar

# **Gamma Knife vs DBS: Clinical**

- **Efficacy appears comparable**
- **Gamma preferred by many pts to open procedures**
- **Gamma less risk acute infection or hemorrhage**
- **Cannot predict radiation sensitivity with gamma with long term risks of cysts and ?neoplasms**
- **DBS reversible**
- **Possible tolerance with DBS**
- **DBS not as cost effective as gamma**
- **Need for battery replacements for DBS**
- **Must be near neuromodulation center for DBS**
- **Long term safety data for DBS not available**

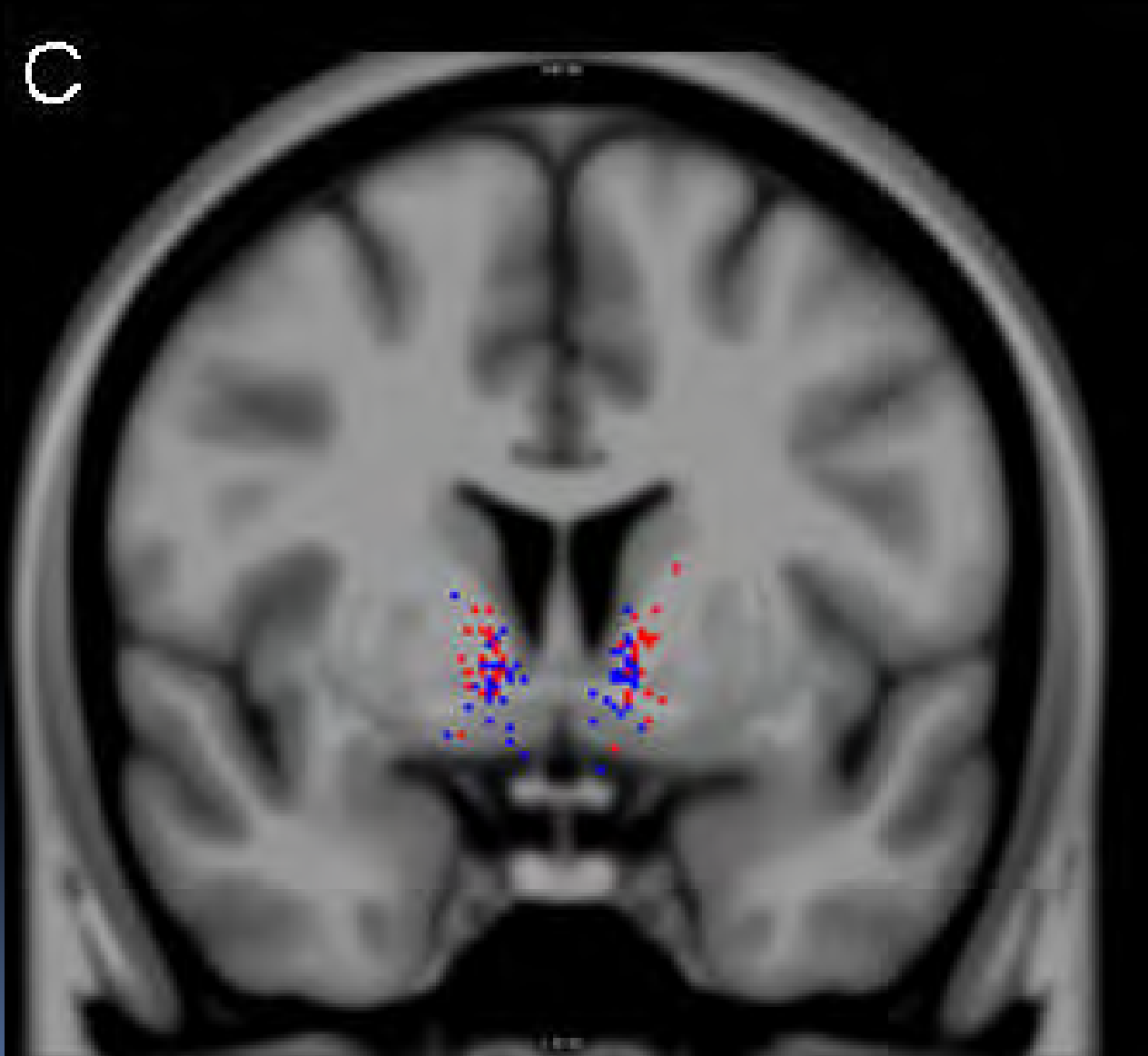








# DTI of Orbital Axons in Anterior Capsule in Normals



## Gamma Ventral Capsulotomy: YBOCS Responder Rates, Staged and Combined Cohorts



Time since surgery	<25%	25-34%	35% +	Total
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### Staged Group\*

6 months	11 (73%)	1 (7%)	3 (20%)	15
1 year	8 (53%)	2 (13%)	5 (33%)	15
2 year	7 (47%)	3 (20%)	5 (33%)	15
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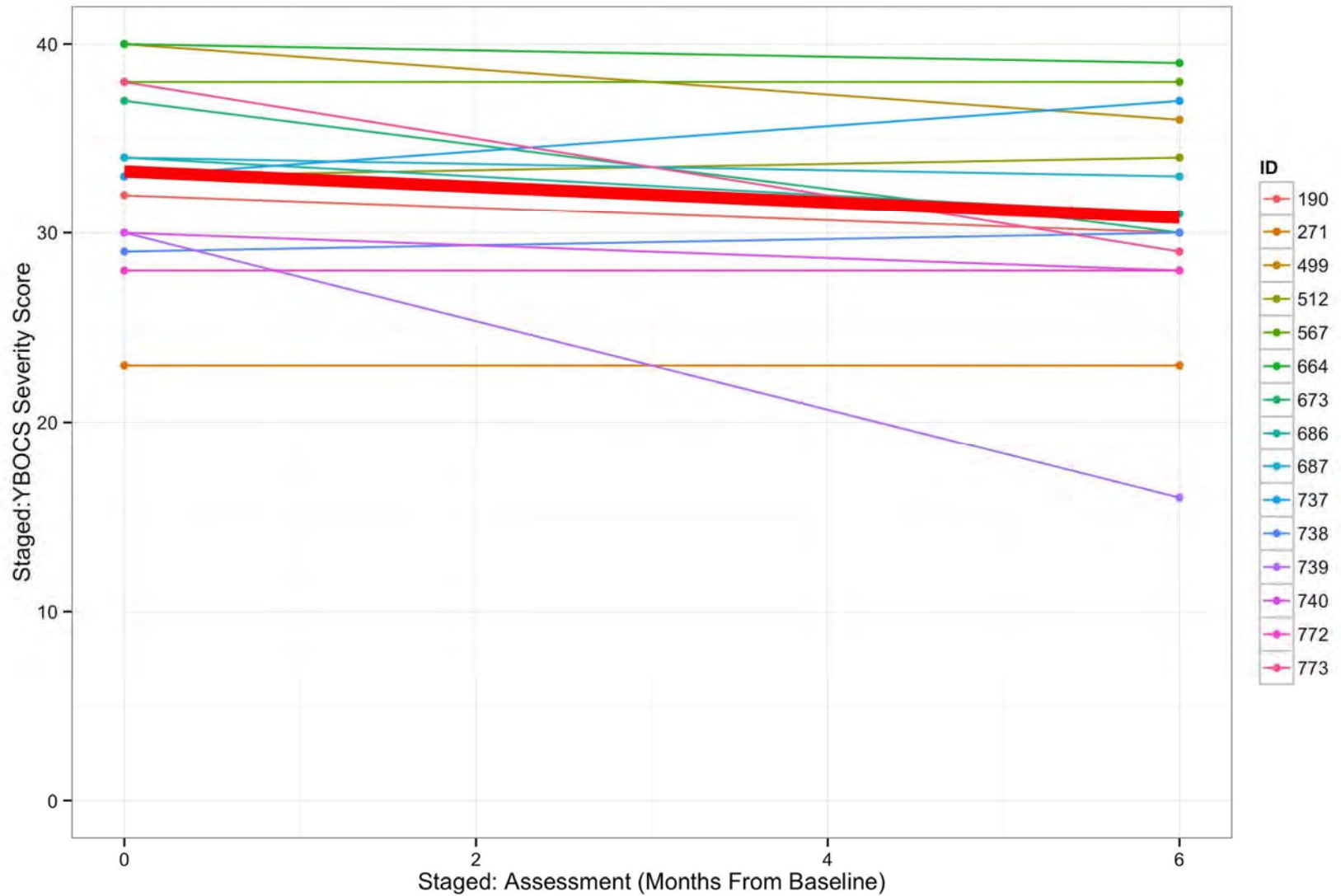
### Combined Group

6 months	21 (53%)	6 (15%)	13 (33%)	40
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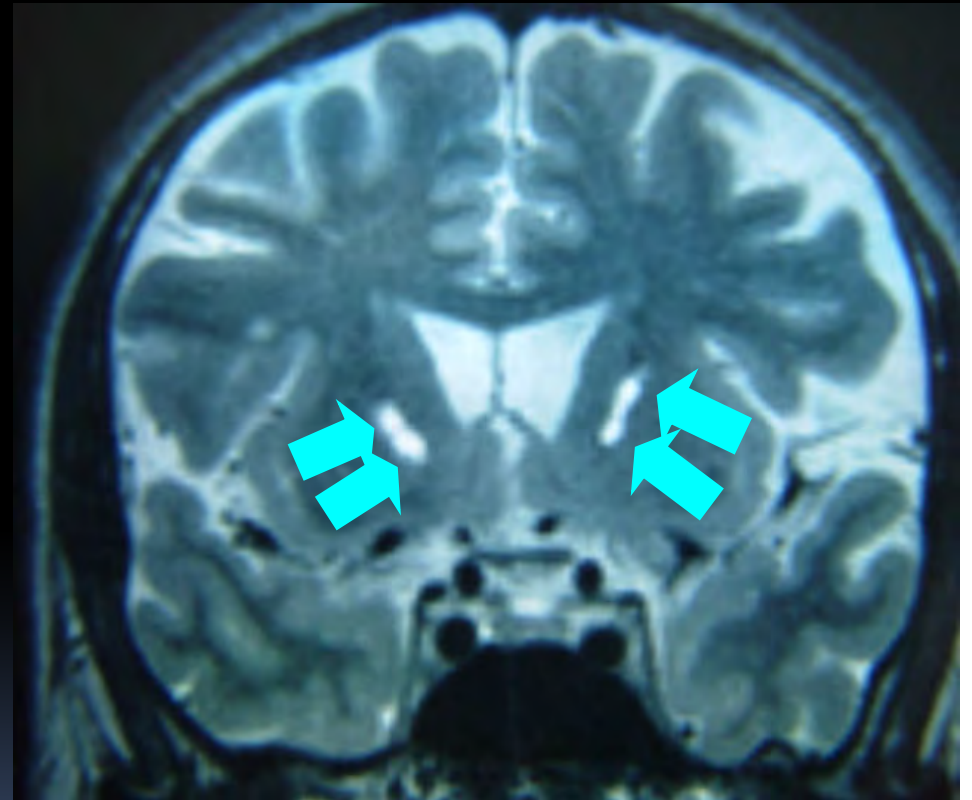


# YBOCS Single Shot Cohort



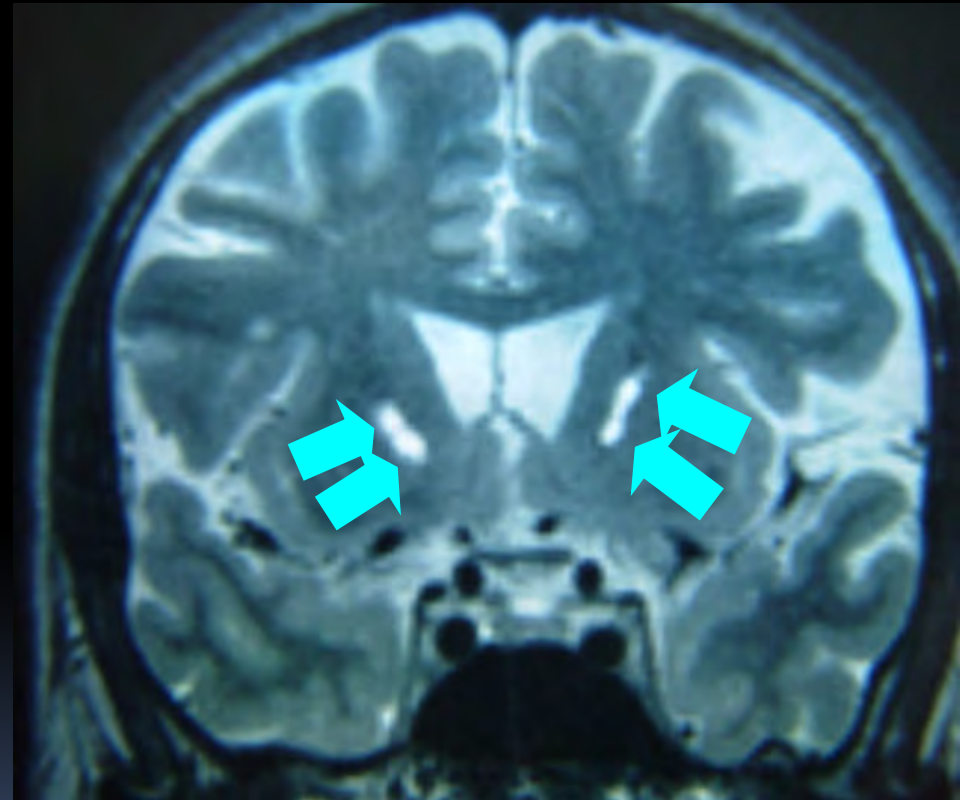
# **“Double-Shot” Gamma Capsulotomy**

- **Two shots bilaterally**
- **65% met response criteria at 2 year followup**

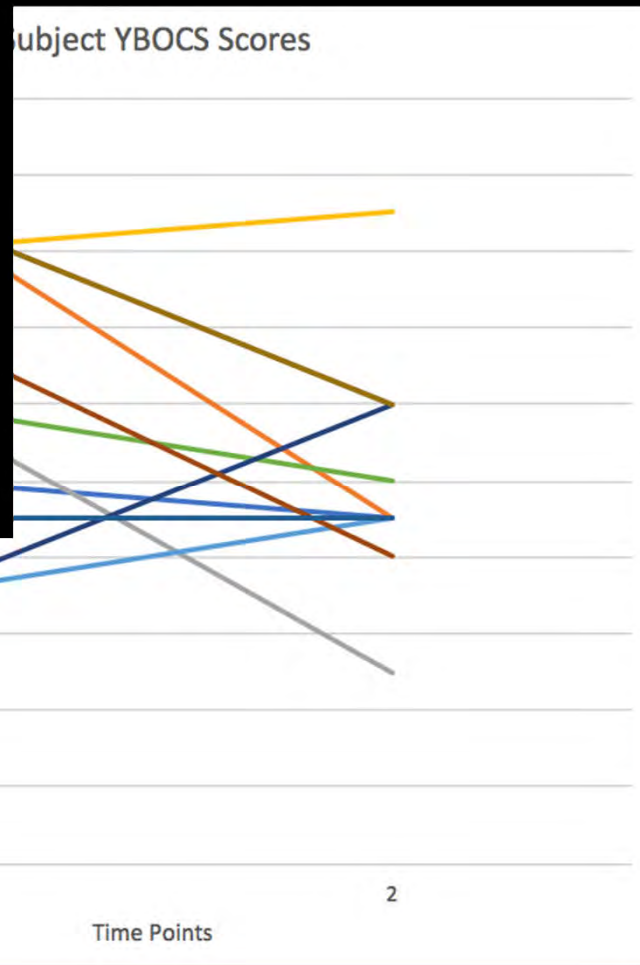
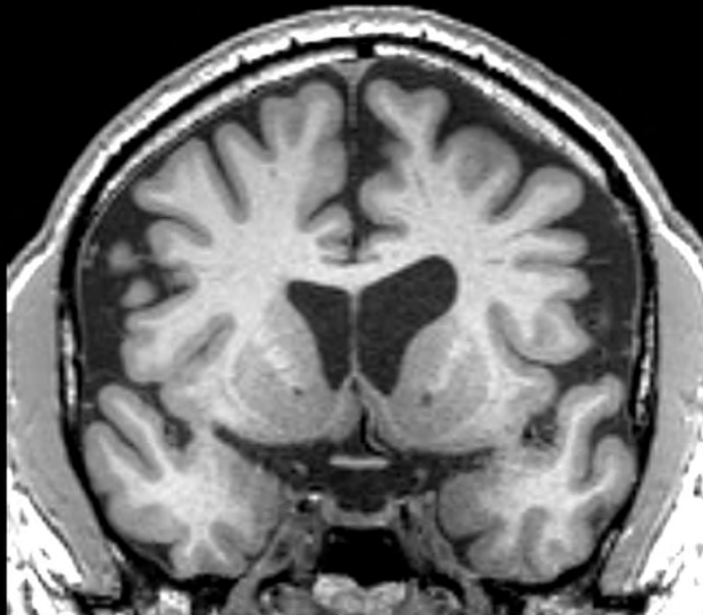


# **“Double-Shot” Gamma Capsulotomy**

- **Two shots bilaterally**
- **65% met stringent response criteria at 2 year followup**



# 'Single Shot' Ventral Gamma Capsulotomy



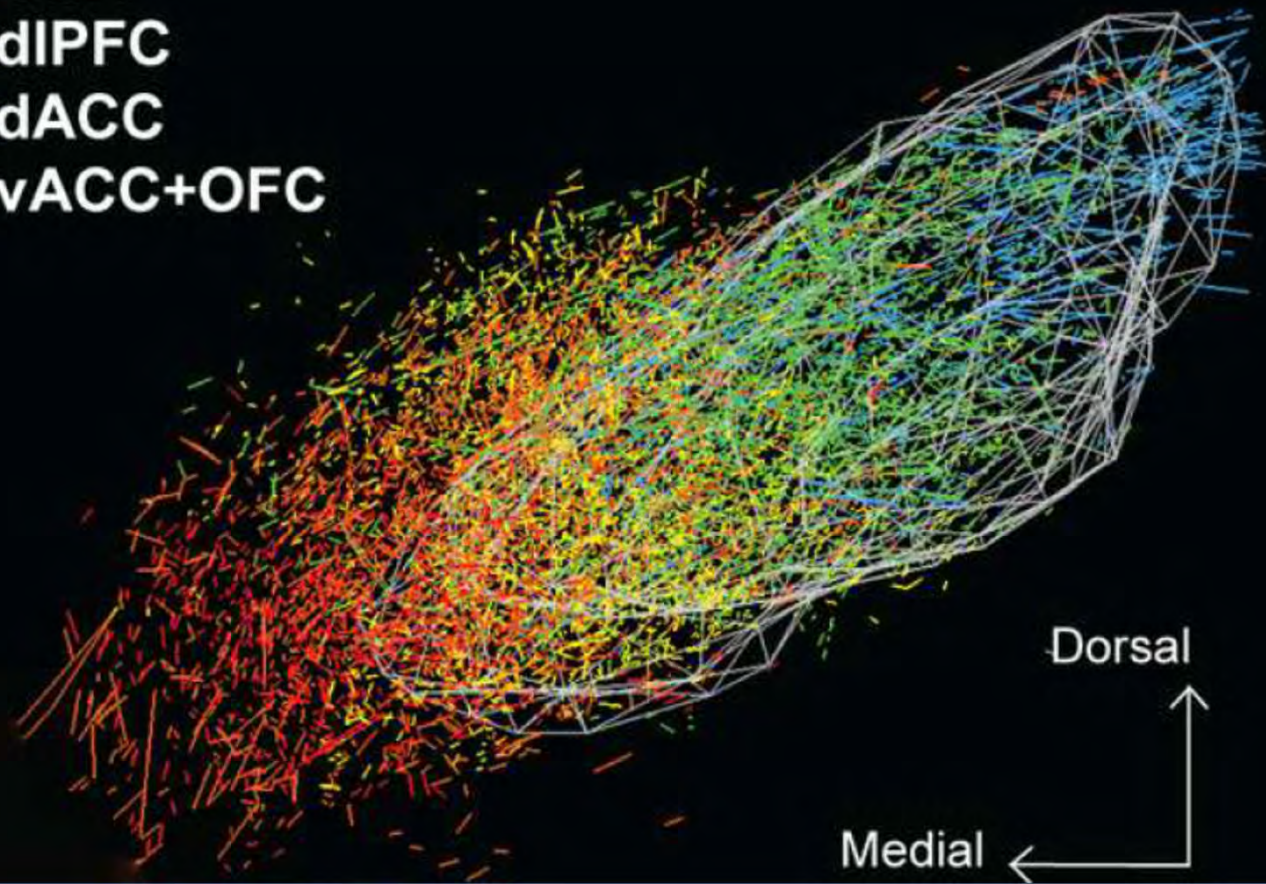
- 11 patients (USP)
- No significant change on Y-BOCS scores at baseline and post-surgery

# Extinction and OCD

- Exposure and response prevention effective for majority of patients
- Success of Exposure Context Dependent
- Variable Rate that Exposure is Learned
- Unclear if strength of fear conditioning or failure of extinction more important
- SSRIs and surgery may enhance extinction recall or diminish fear recall

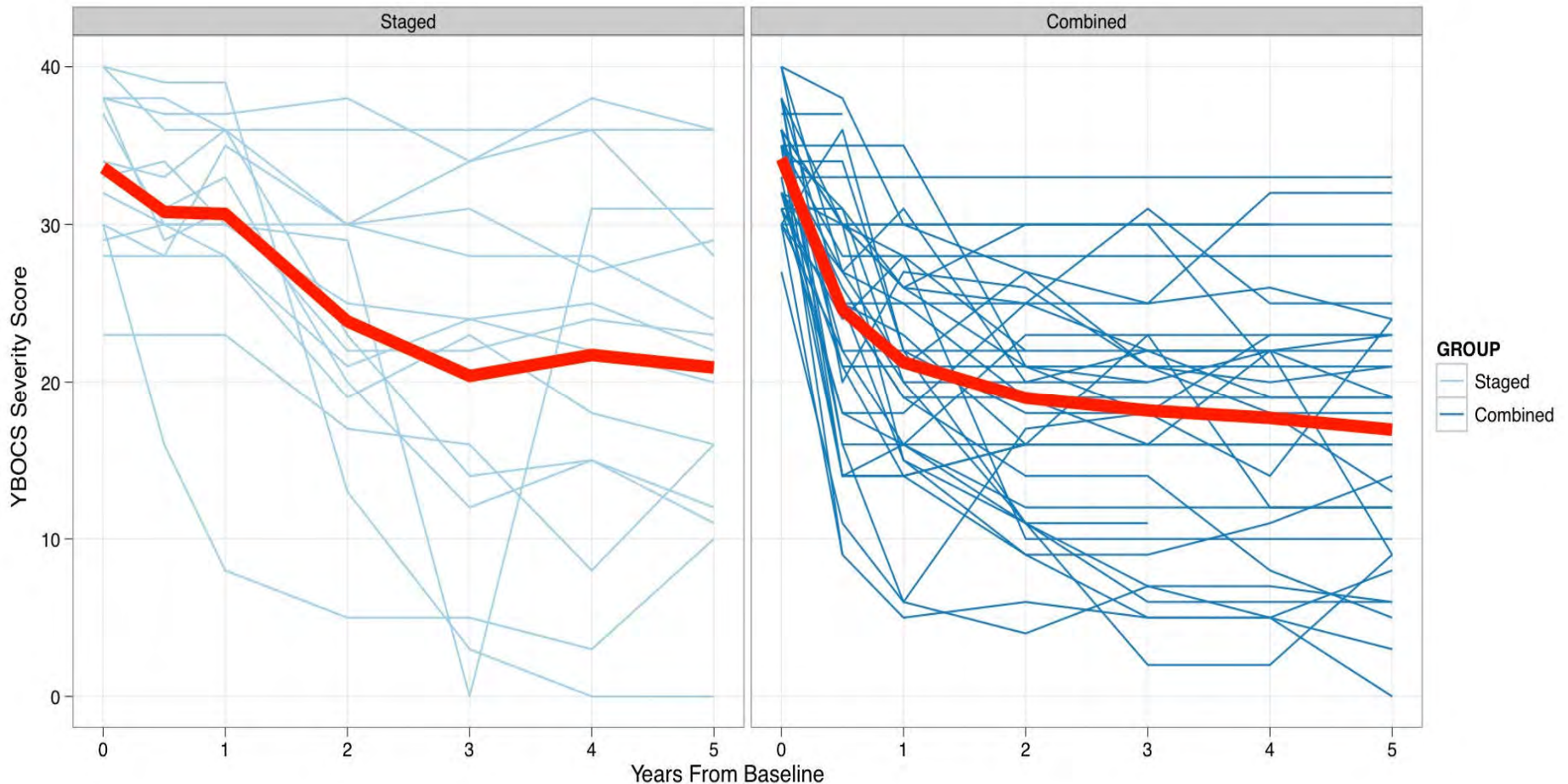
# Corticofugal Fibres through

-  M1
-  SMA
-  dIPFC
-  dACC
-  vACC+OFC



Haber et al

# YBOCS after Staged or Combined Gamma Ventral Capsulotomy

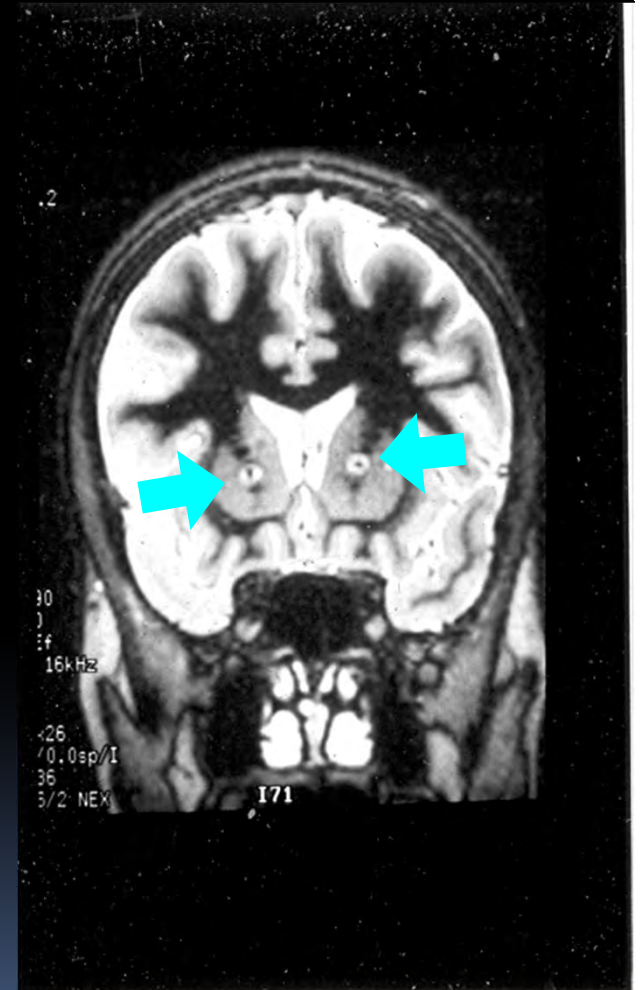


Analyses for Combined: Significant reductions over time:  
 $B=-2.68$   $SE=0.29$ ;  $p= 0.0000$ ;  
No effect of Age on outcomes:  $B=0.03$ ;  $SE= 0.07$ ;  $p= 0.62$

# Gamma Knife Capsulotomy

## First Method

- **Bilateral single “shots” in the middle of the anterior capsule**
- **Only 1/15 patients very much improved**
- **Later, a second pair of more ventral lesions added in 13 of 15 patients**

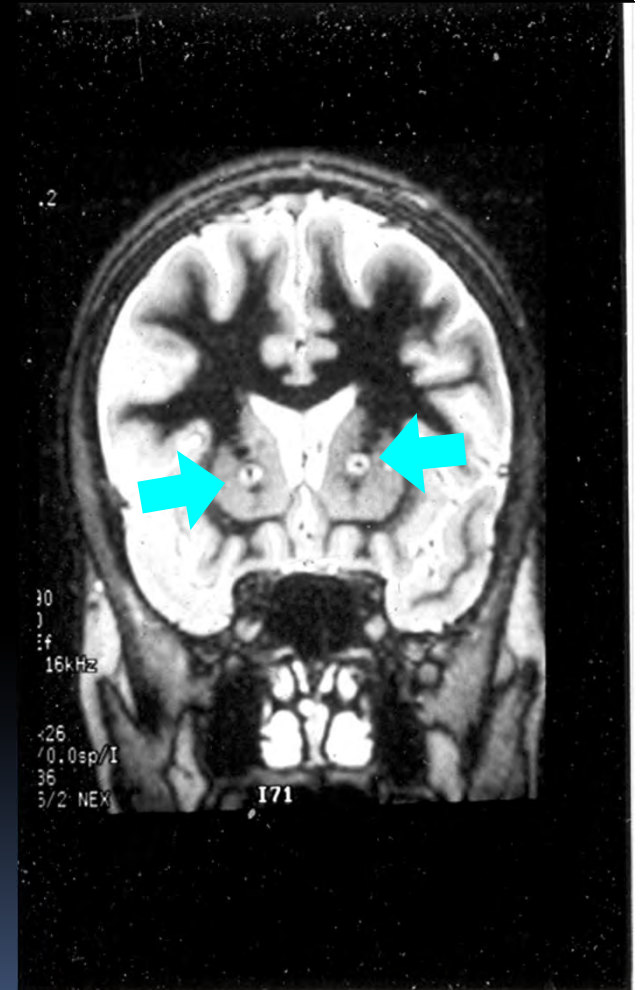


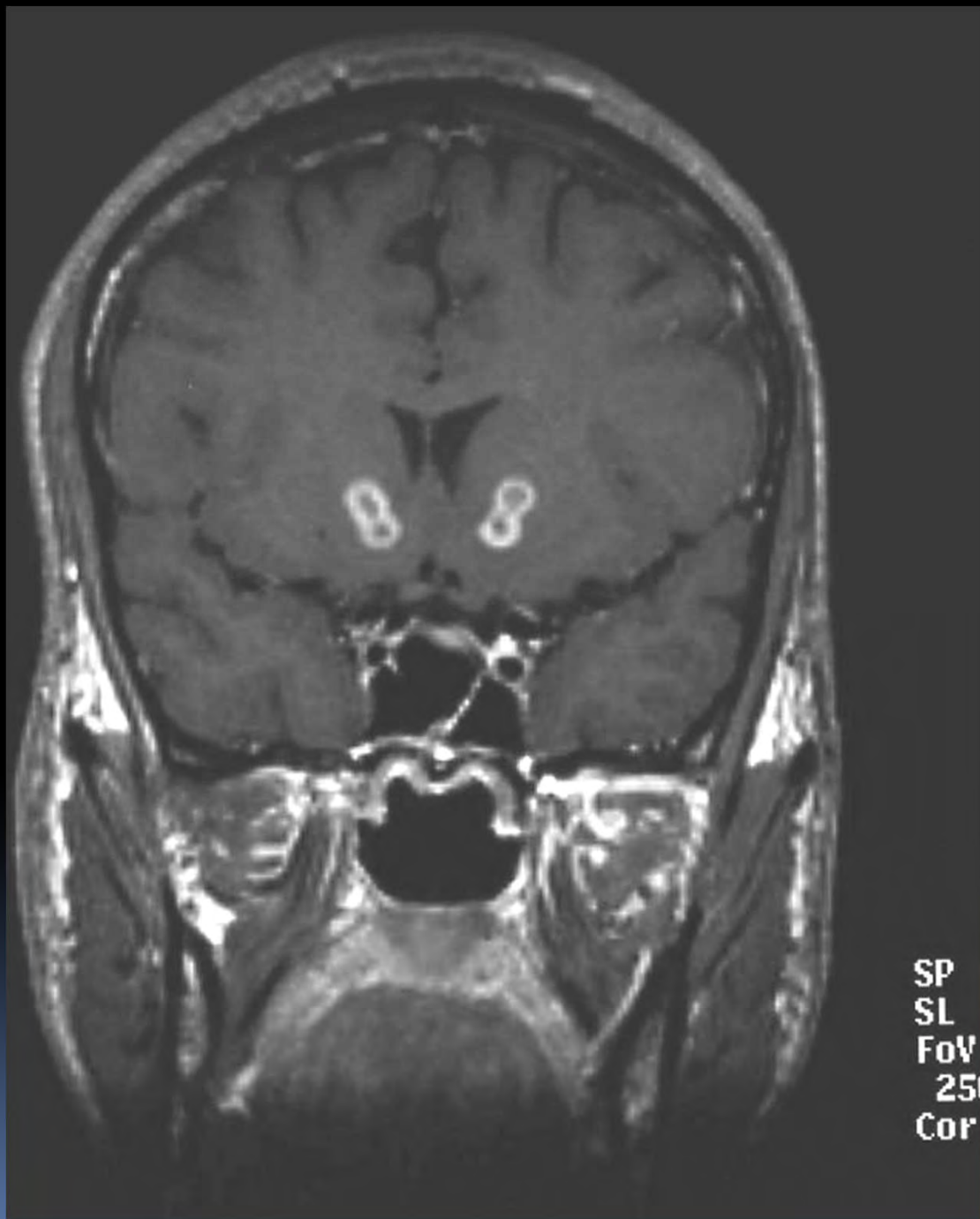


# Gamma Knife Capsulotomy

## First Single Shot Cohort

- **Bilateral single “shots” in the middle of the anterior capsule**
- **Only 1/15 patients very much improved**
- **Later, a second pair of more ventral lesions added in 13 of 15 patients**



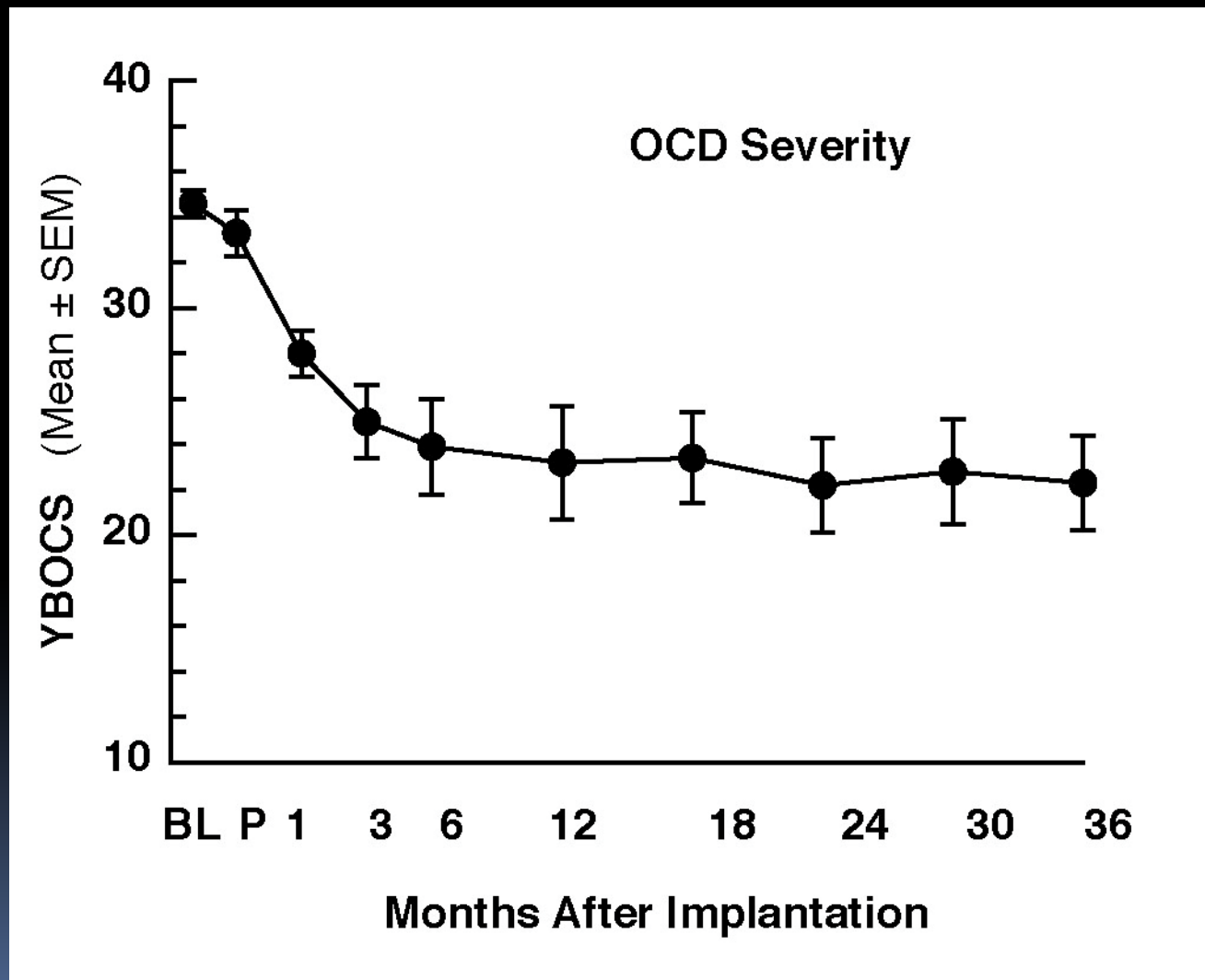


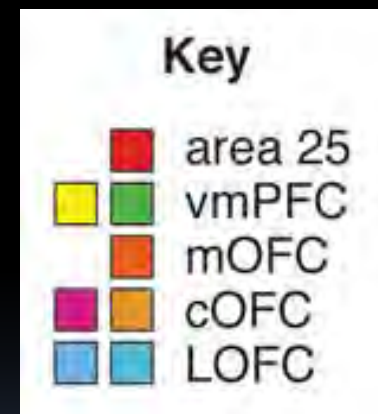
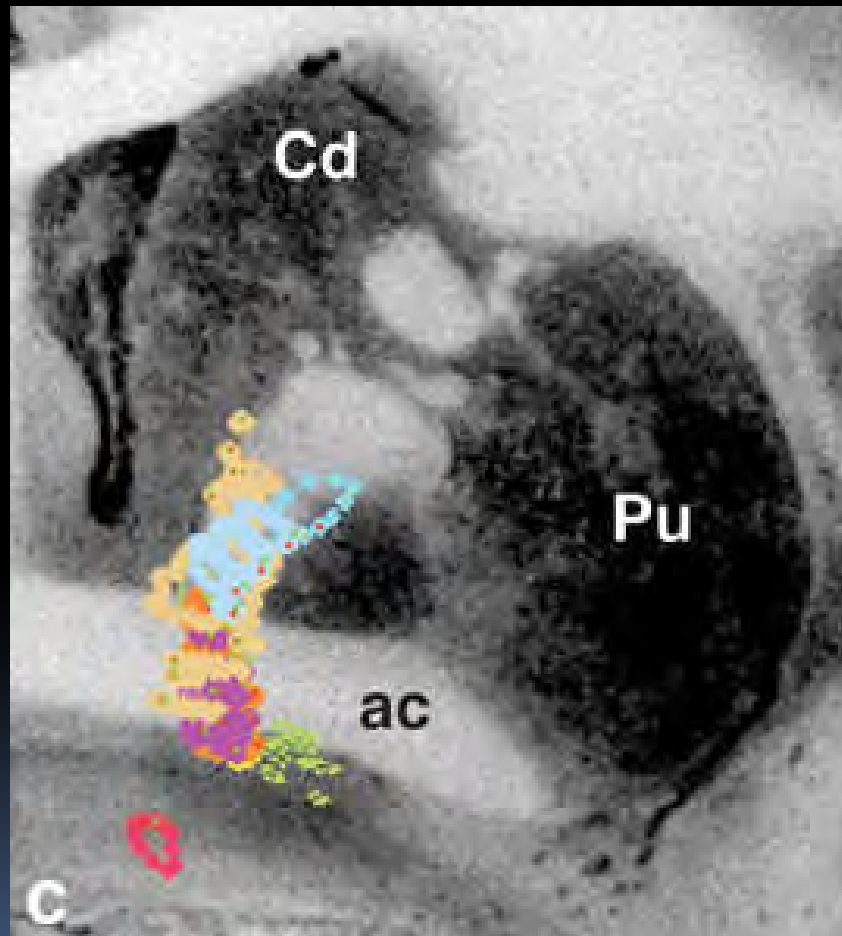
SP  
SL  
FoV  
250  
Cor



Sham

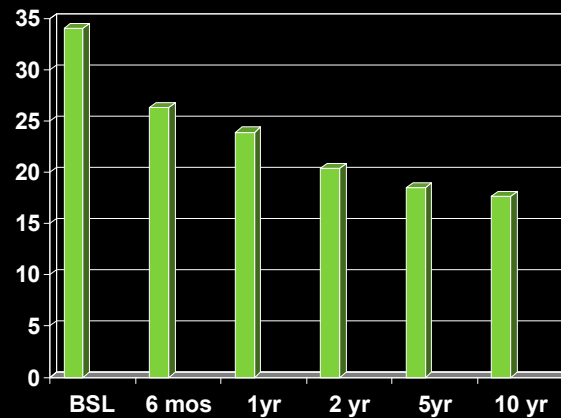
# Long-term outcomes





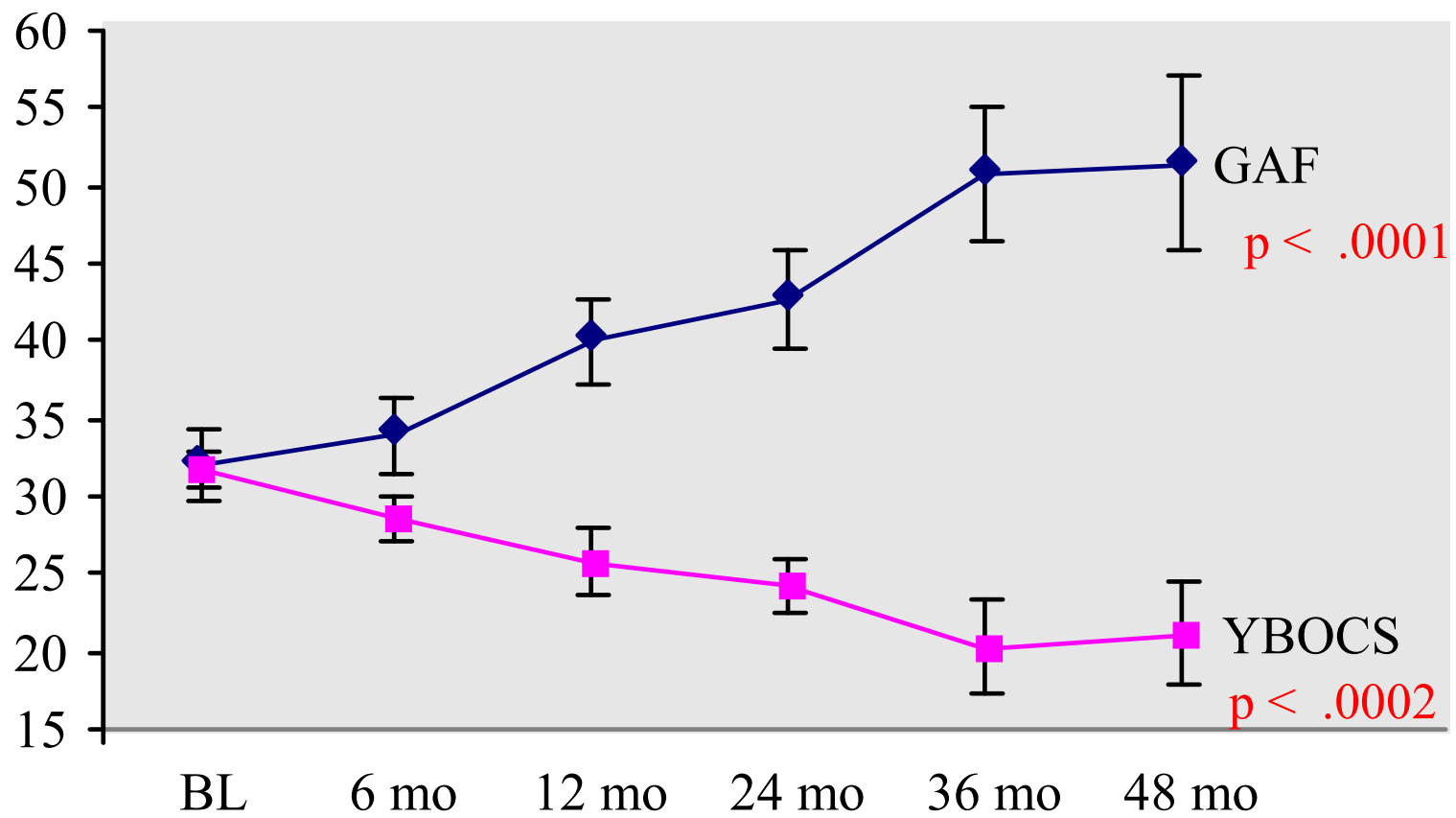
Haber et al 2010

# Gamma Knife Capsulotomy: 10 Yr Followup Carry Forward Analysis

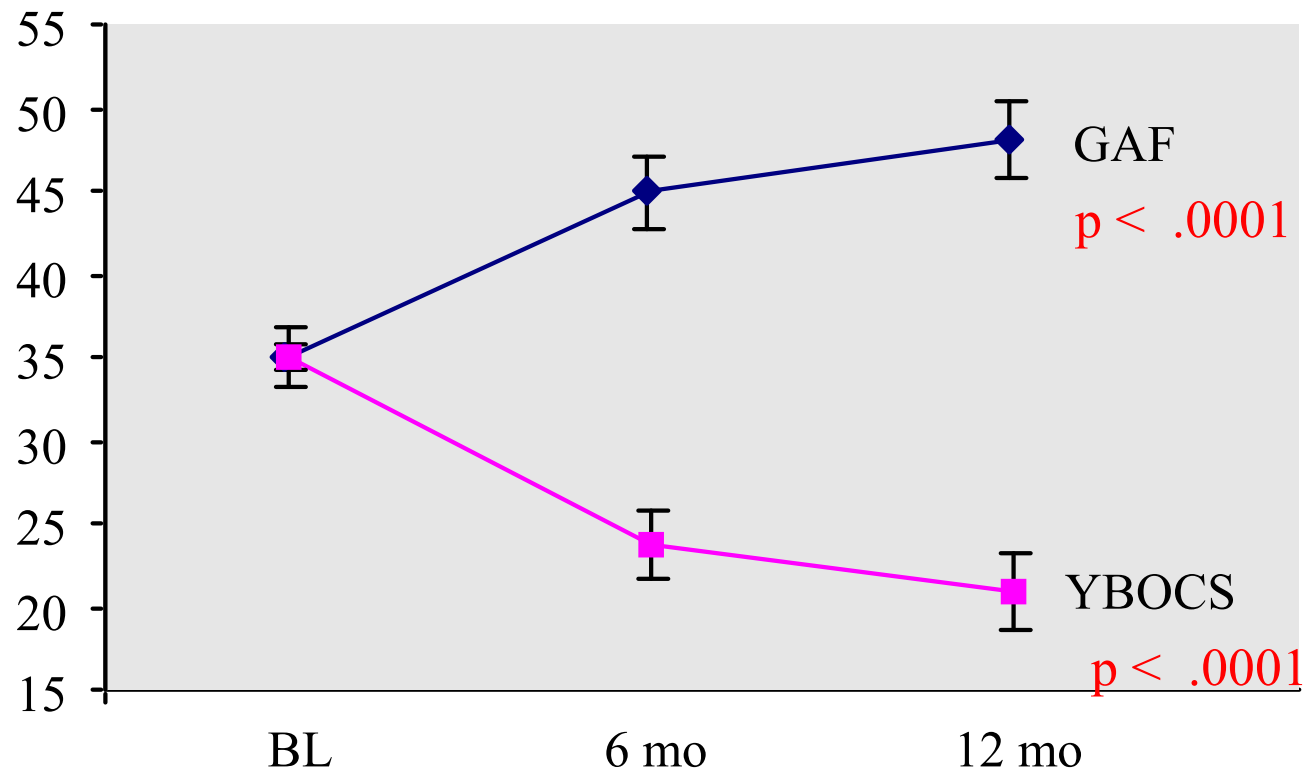


Y  
B  
D  
C  
C  
S

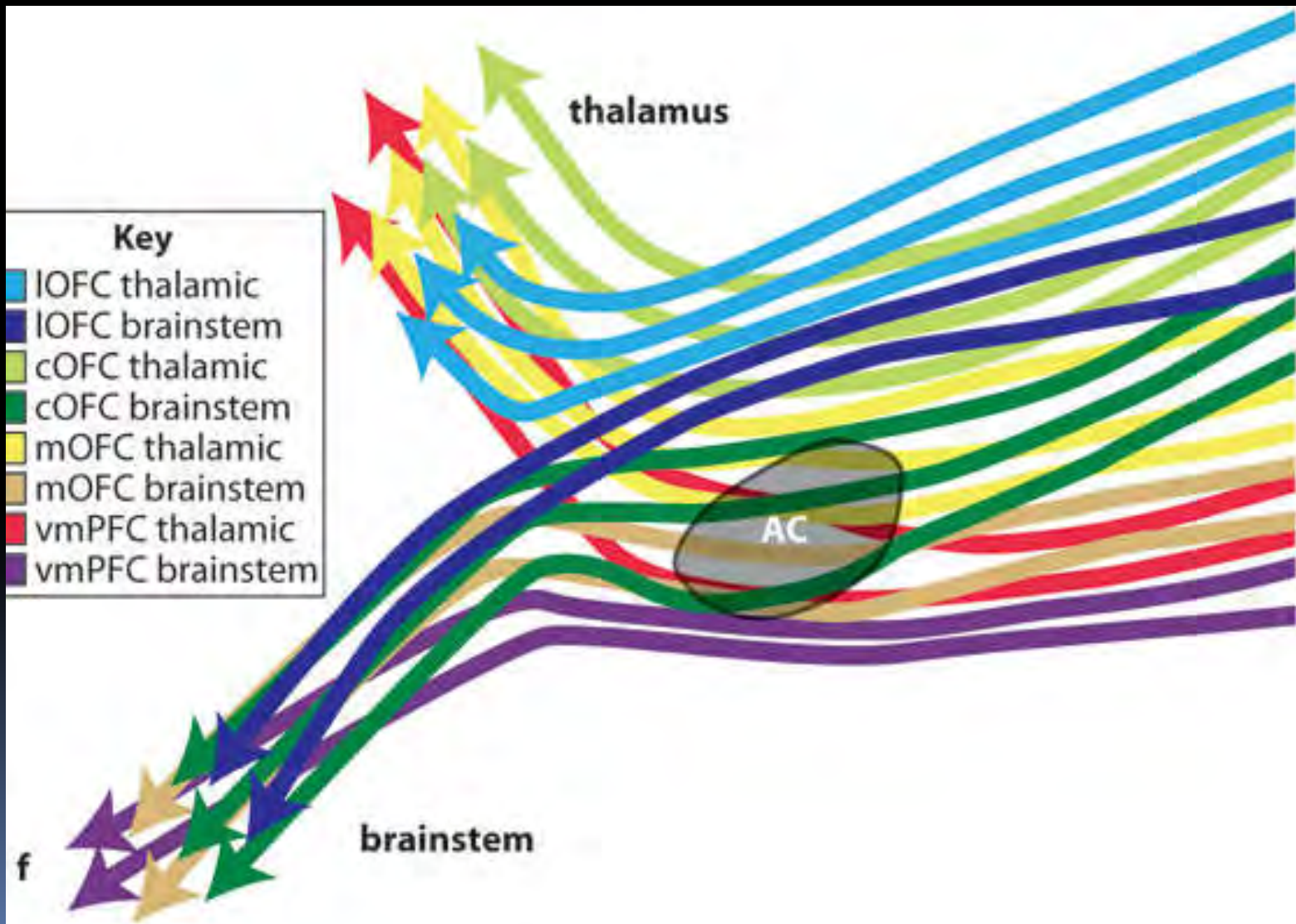
# Gamma Capsulotomy Efficacy: Two Stage Lesions (YBOCS & GAF)



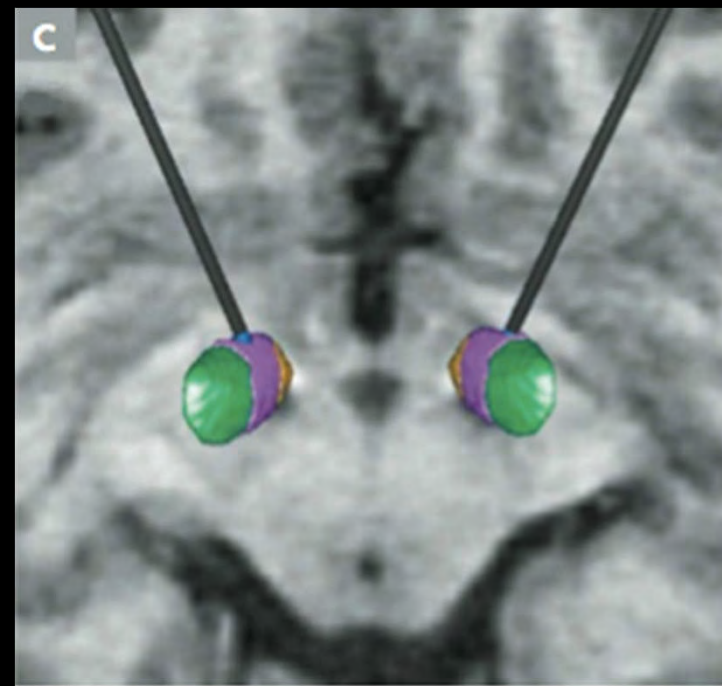
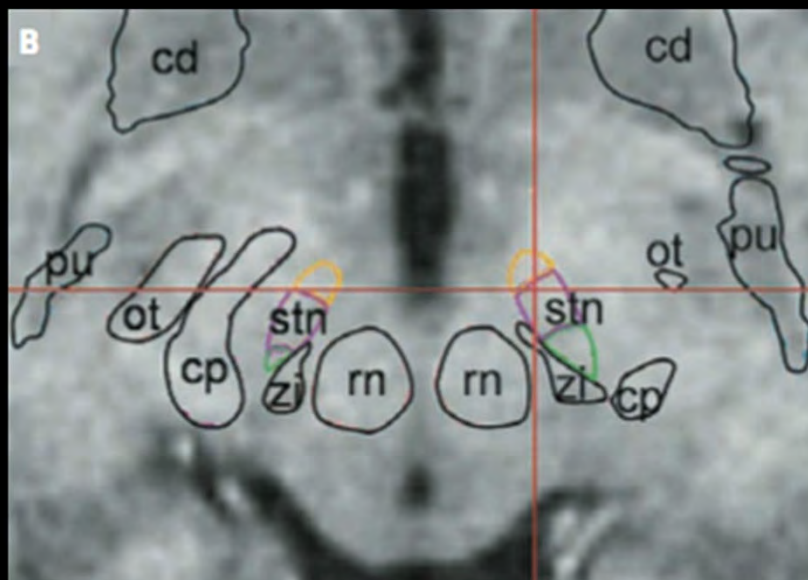
# Gamma Capsulotomy Efficacy: Double Shot (YBOCS & GAF)







# STN DBS in OCD



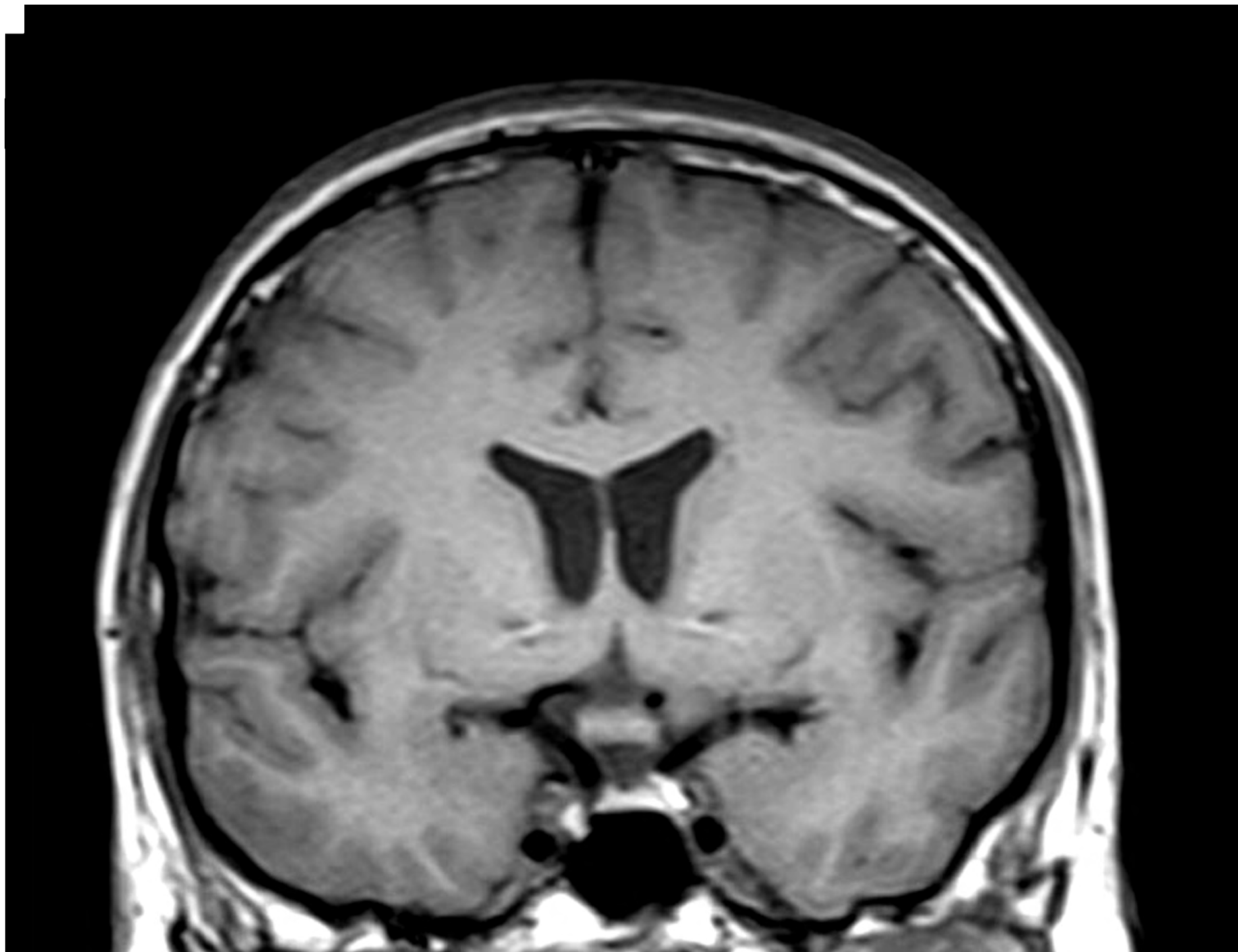
Mallet et al, 2008

**While some fears  
may be innate,**



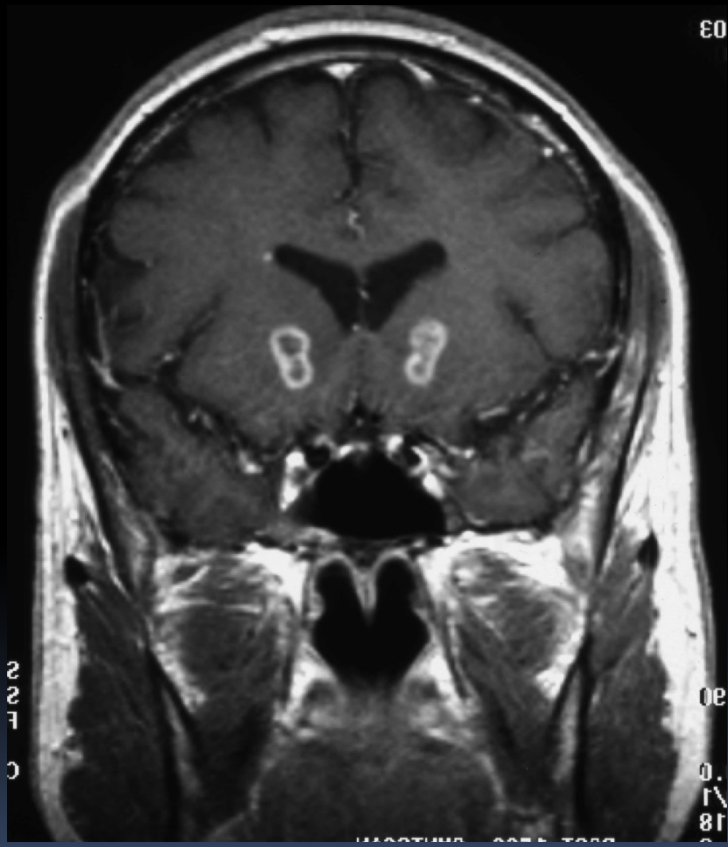
**most fears are  
learned through  
conditioning or  
instruction.**



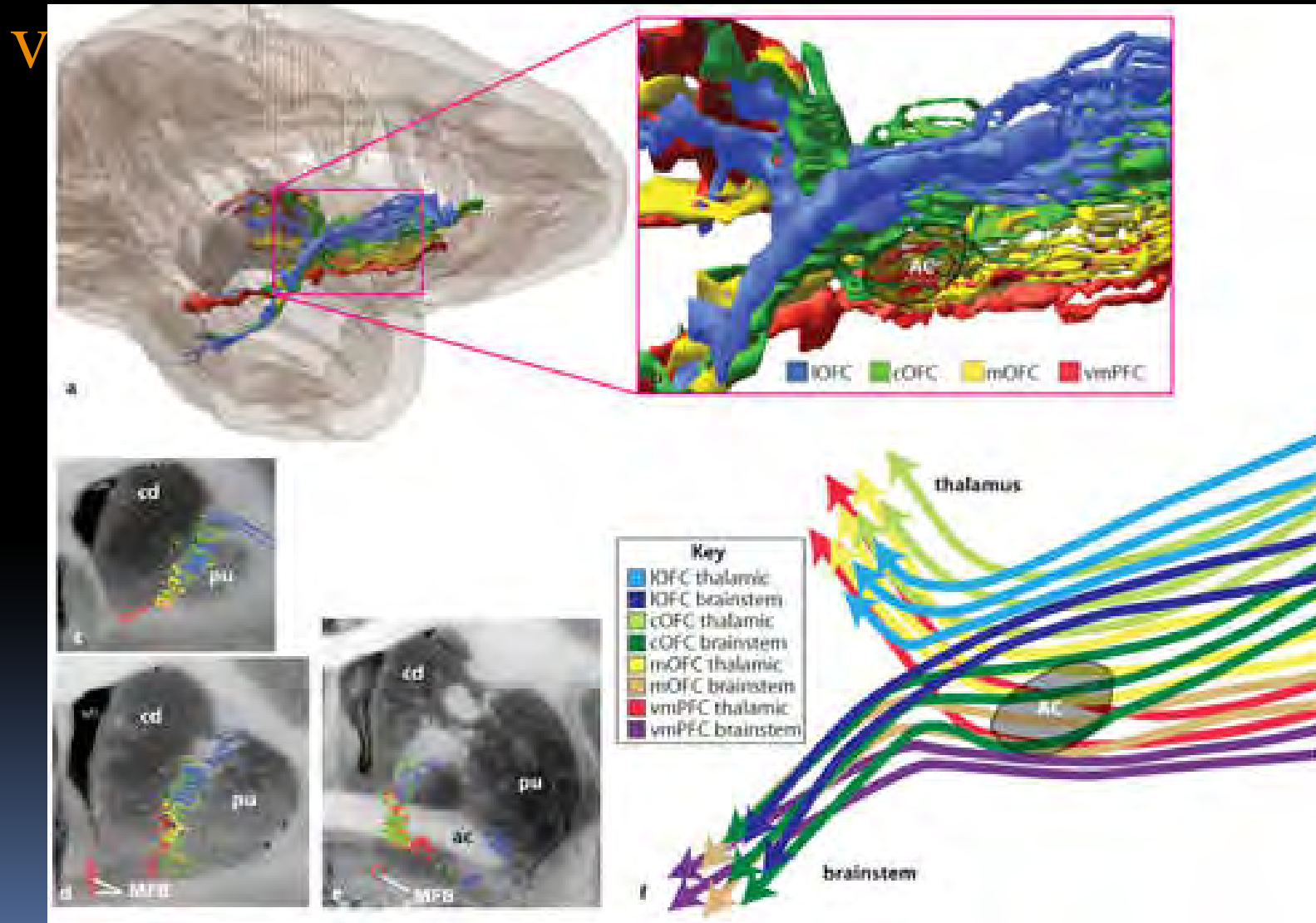


# Extinction and OCD

- Exposure and response prevention effective for majority of patients
- Success of Exposure Context Dependent
- Variable Rate that Exposure is Learned
- Unclear if strength of fear conditioning or failure of extinction more important
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# Figure 5: Schematics and coronal sections of the global model illustrating the





**“By continually repeating the order to perform the feared action, that is, exposure, he will help the patient greatly by words of encouragement at every sign of success, however insignificant, for encouragement will make the patient realize these little successes and will stimulate him with the hopes aroused by glimpses of greater successes in the future.”**

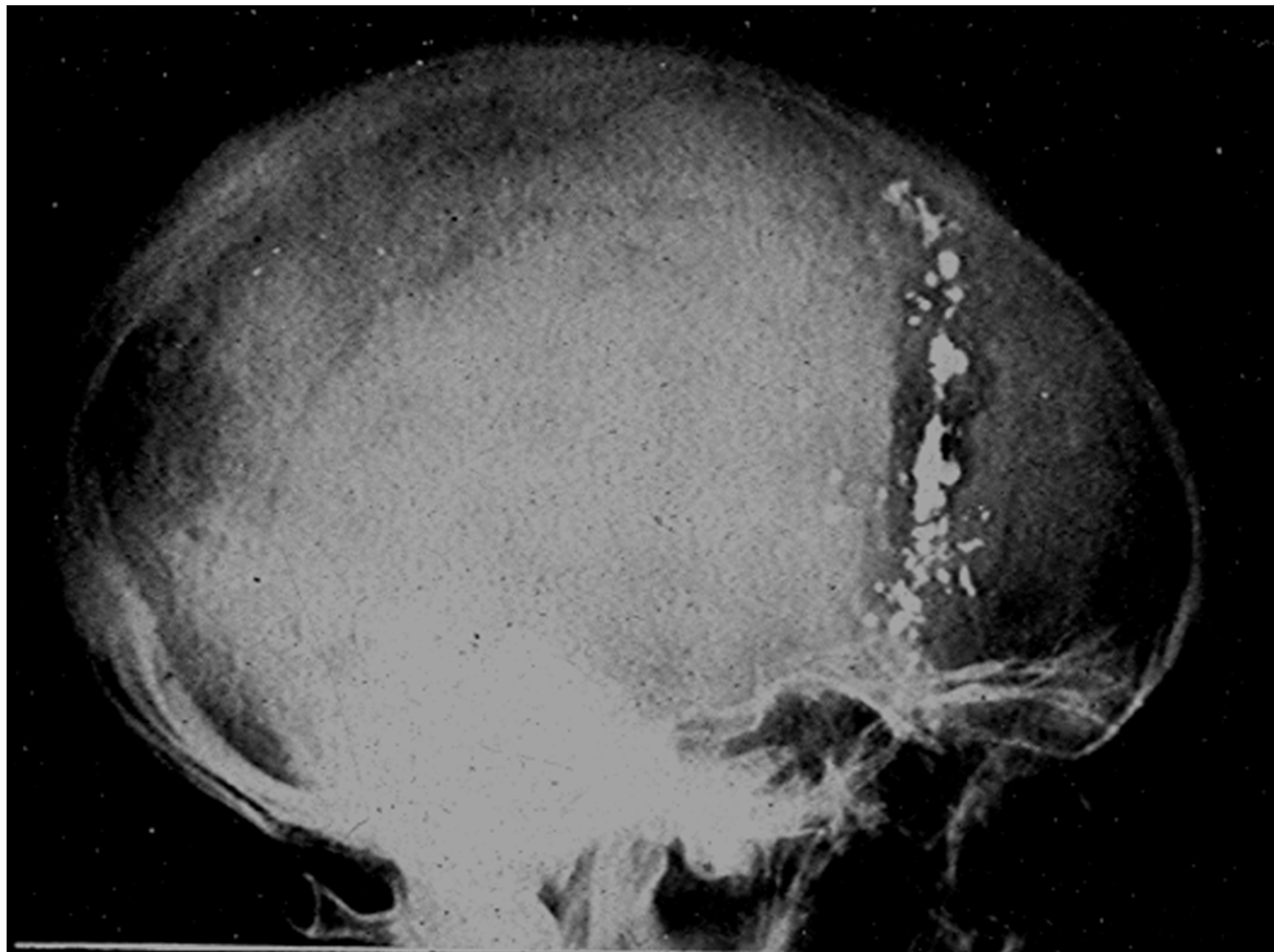
**Janet 1904**



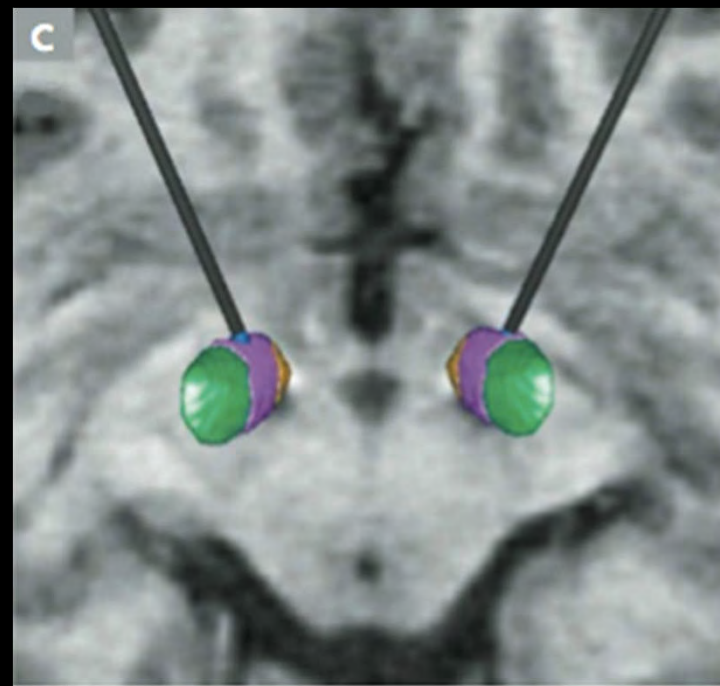
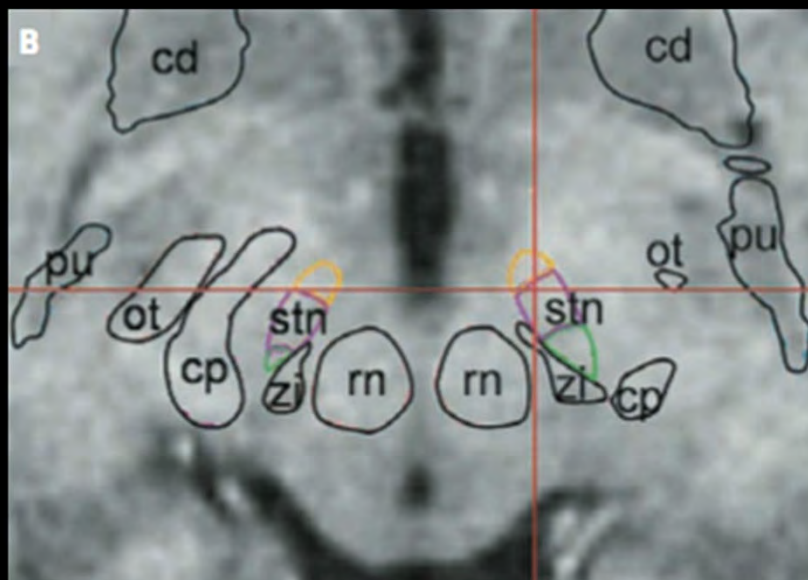
“ It is necessary to alter these synapse adjustments and change the path chosen by the impulses in their constant passage so as to modify corresponding ideas and force thoughts into different channels...By upsetting the existing adjustments and setting in movement in other [connections]. I [Expect] to be able to transform the psychic reactions and to relieve the patient thereby”

- Egas Moniz (1935)





# STN DBS in OCD



Mallet et al, 2008

DLPFC  
Frontal Pole  
Cognitive Control  
Planning

Dorsolatera  
|  
Caudate

rGPI

Parvocellular  
DMNT

mPFC  
Action selection  
Starting- Stopping  
Task Switching

Dorsomedial  
Caudate

GPI  
SNR

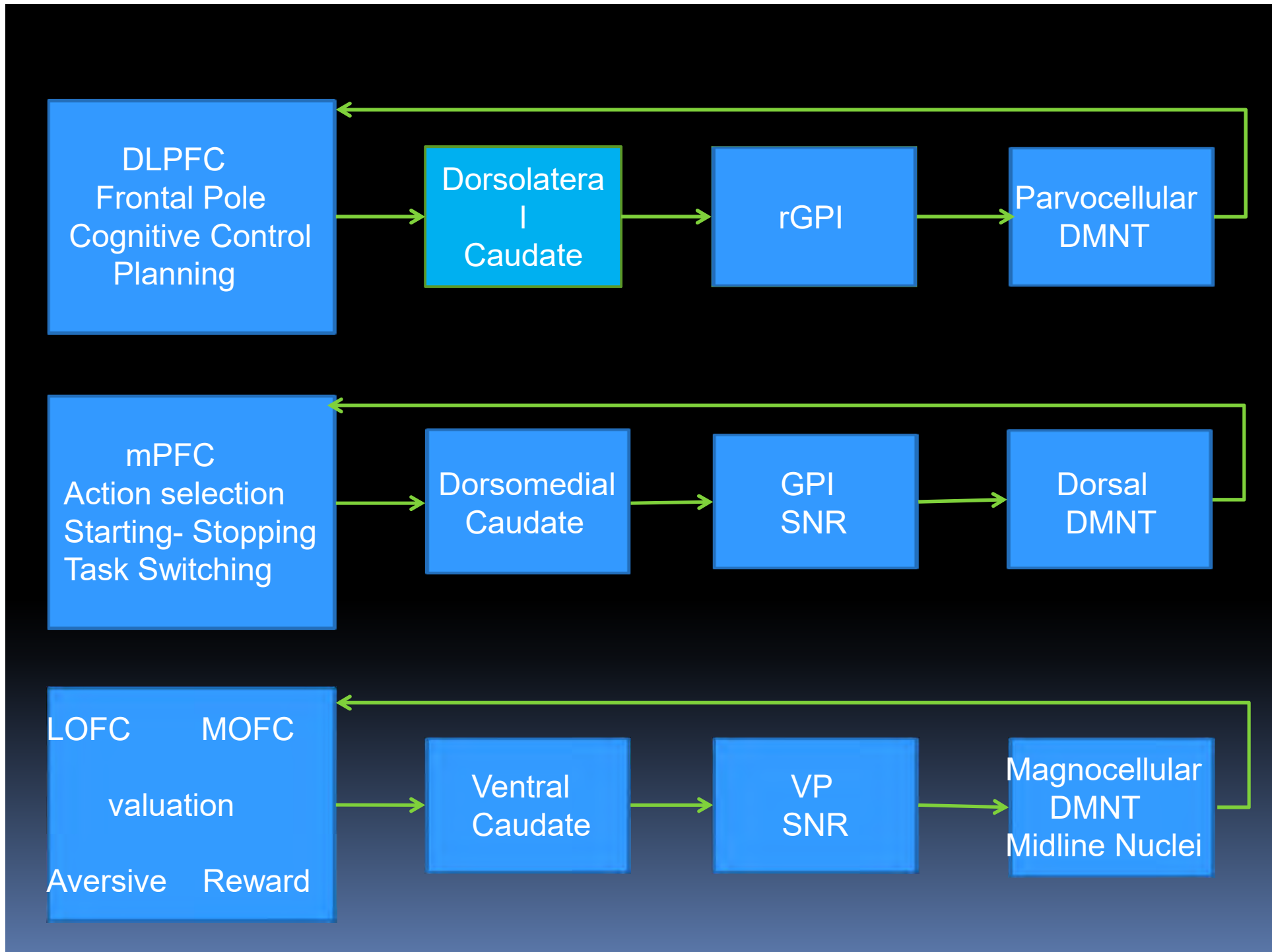
Dorsal  
DMNT

LOFC      MOFC  
valuation  
Aversive    Reward

Ventral  
Caudate

VP  
SNR

Magnocellular  
DMNT  
Midline Nuclei



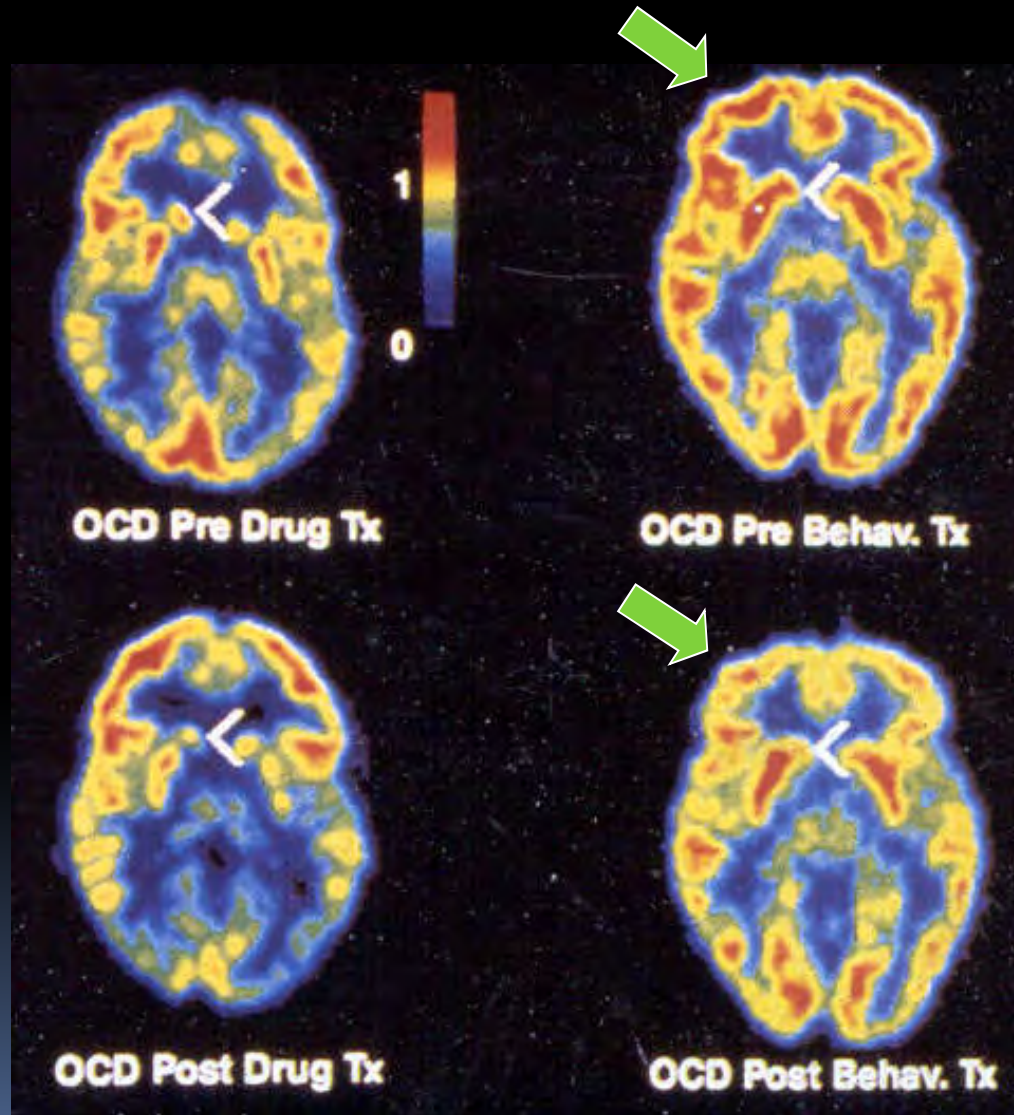


# OCD: Metabolic Changes after Treatment

Pre

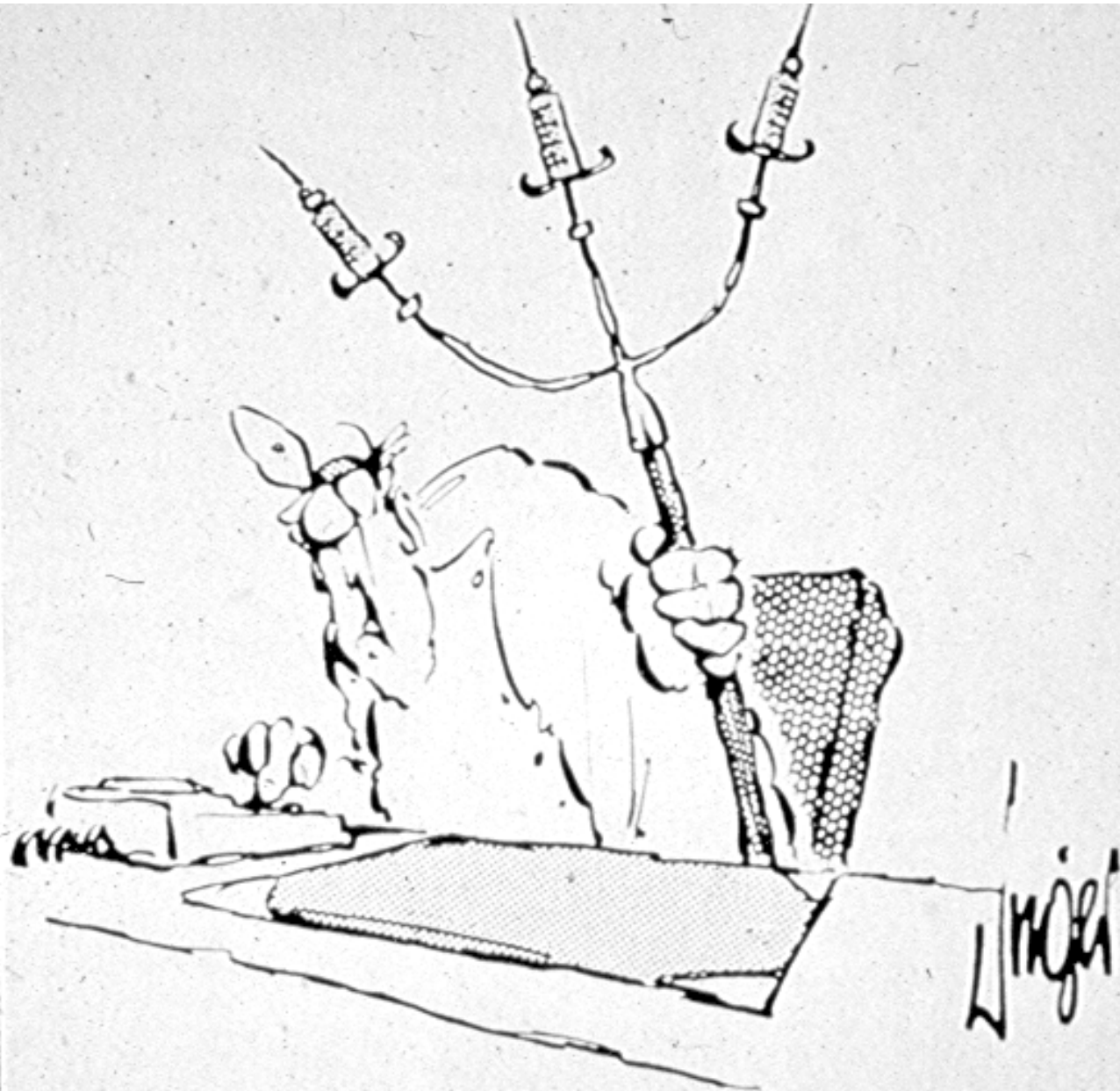


Post



Drug

BT



"Send in the next three patients."

