

BRAIN AND BEHAVIOR BASED STRATEGIES IN THE TREATMENT OF OCD

Christopher Pittenger, MD, Ph.D.

Director, Yale OCD Research Clinic

Assistant Chair for Translational Research, Yale University Dept of Psychiatry

Associate Professor of Psychiatry and in the Yale Child Study Center

International OCD Foundation Scientific Advisory Board: Chair, Annual IOCDF Research Symposium;
Chair, IOCDF Grant Review Committee; Member, IOCDF Clinical and Scientific Advisory Board

Past recipient, NARSAD Young Investigator Award (2007, 2010), NARSAD Independent Investigator
Award (2016)

OUTLINE OF TODAY'S TALK

- Phenomenology, diagnosis, epidemiology
- Neural underpinnings
- A framework for understanding obsessions and compulsions
- Psychotherapy for OCD: Symptom evocation and ritual prevention (ERP)
- Pharmacological treatment of OCD: serotonin reuptake inhibitors
- New directions in pharmacological treatment: Glutamate modulators and psychedelics
- New directions in therapy: Neurofeedback

CONFLICTS

- Research funding from NIMH, NINDS, BBRF, IOCDF, Simons Foundation, Doris Duke Charitable Foundation, Taylor Family Foundation, MGH Research Fund
- Current clinical trial funded by Biohaven Pharmaceuticals
- Consultant to Biohaven Pharmaceuticals, Teva Pharmaceuticals, Blackthorn Therapeutics, Brainsway Therapeutics
- Royalties from Oxford University Press, Elsevier Ltd
- Patent on near infrared spectroscopy neurofeedback for the treatment of anxiety

I am not obsessive

I am not obsessive

I am not obsessive

I am NOT OBSESSIVE

I AM not obsessive

I am not OBSESSIVE

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OBSESSIVE-COMPULSIVE DISORDER: PHENOMENOLOGY, DIAGNOSIS, EPIDEMIOLOGY

- **OBSESSIONS** – Recurrent and persistent thoughts, images, or urges that are experienced as intrusive or unwanted and that typically produce marked anxiety or distress
 - The sufferer tries to ignore or suppress the thoughts, urges, or impulses or to neutralize them with some other thought or action



OBSESSIVE-COMPULSIVE DISORDER: PHENOMENOLOGY, DIAGNOSIS, EPIDEMIOLOGY

- **COMPULSIONS** – Repetitive behaviors or mental acts that an individual feels driven to perform in response to an obsessions, or according to rules that must be applied rigidly
 - Performing compulsions is aimed at preventing or reducing anxiety or distress



OBSESSIVE-COMPULSIVE DISORDER: PHENOMENOLOGY, DIAGNOSIS, EPIDEMIOLOGY

- Lifetime morbid risk of 2.7% (Kessler et al, 2012)
- One-year prevalence of 1.3% (Kessler et al, 2012)
- 10th cause of morbidity, worldwide, in 1996 Global Burden of Disease study from WHO
- Most commonly severe of any of the DSM-IV anxiety disorders (Ruscio et al, 2010)
- Diagnosis is often missed or delayed; appropriate treatment is often not available
- ~25% of cases are refractory to the best available evidence-based treatments



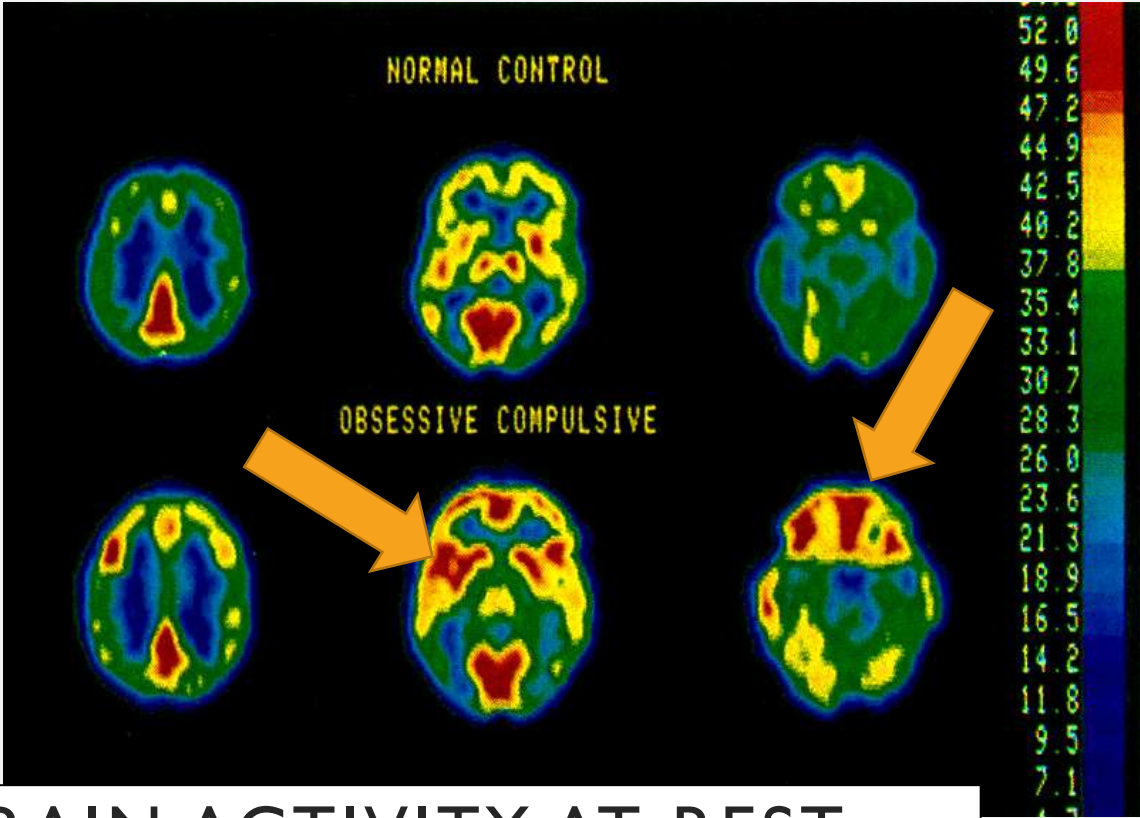
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OBSESSIVE-COMPULSIVE DISORDER: NEURAL UNDERPINNINGS



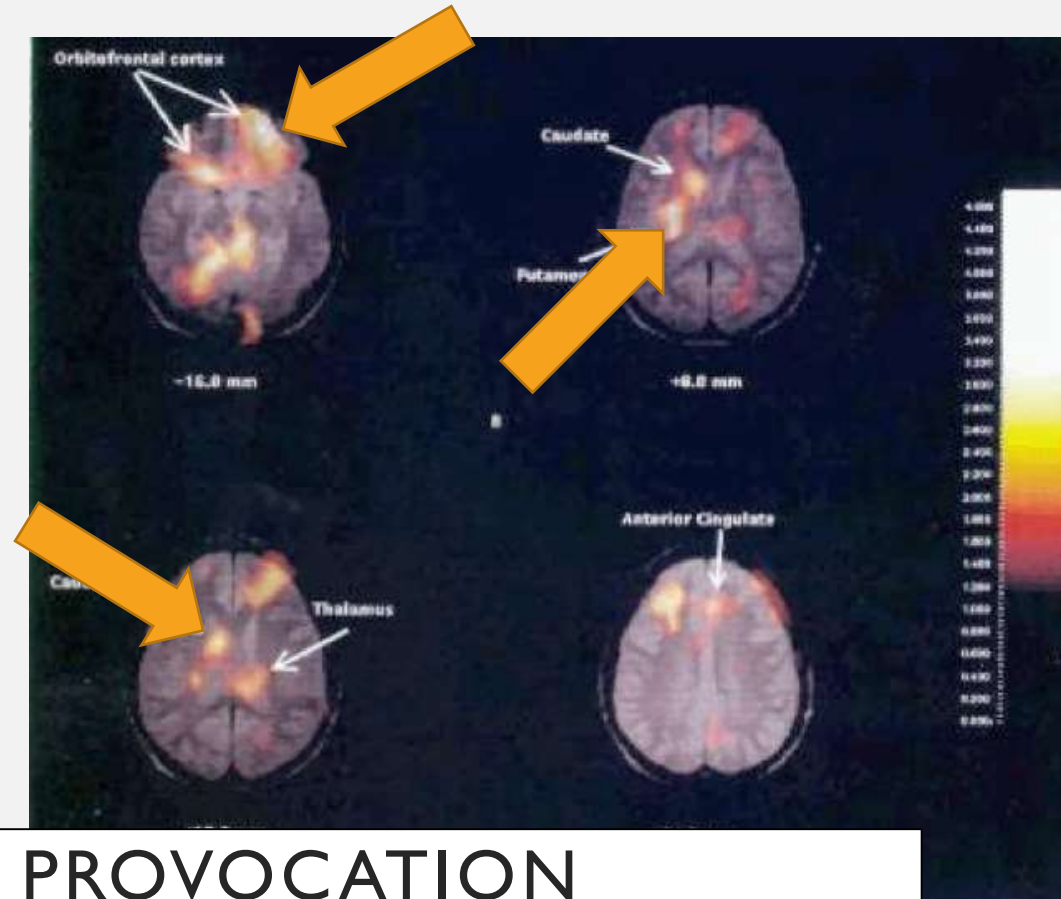
OBSESSIVE-COMPULSIVE DISORDER: NEURAL UNDERPINNINGS



INCREASED BRAIN ACTIVITY AT REST

Baxter et al, 1987

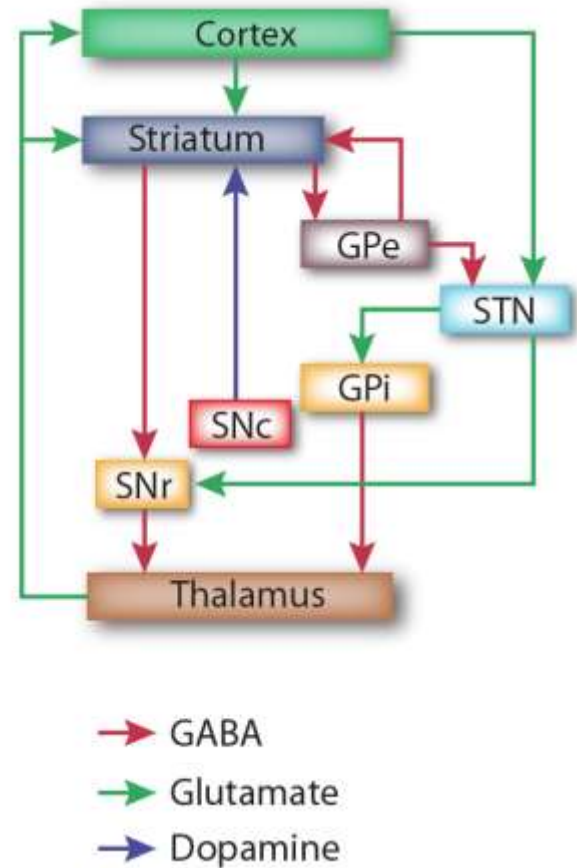
OBSESSIVE-COMPULSIVE DISORDER: NEURAL UNDERPINNINGS

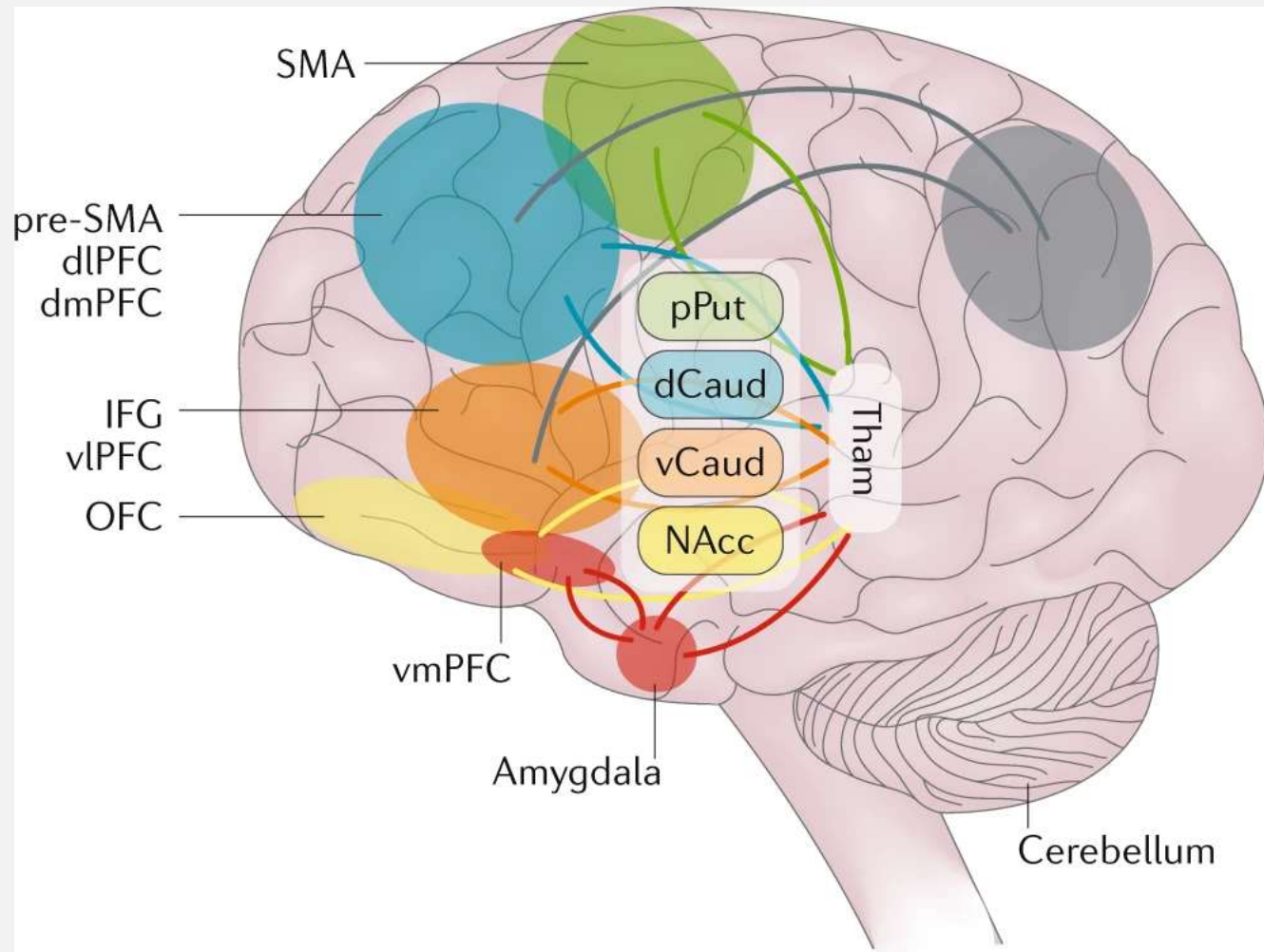


SYMPTOM PROVOCATION

Rauch et al, 1994

OBSESSIVE-COMPULSIVE DISORDER: NEURAL UNDERPINNINGS



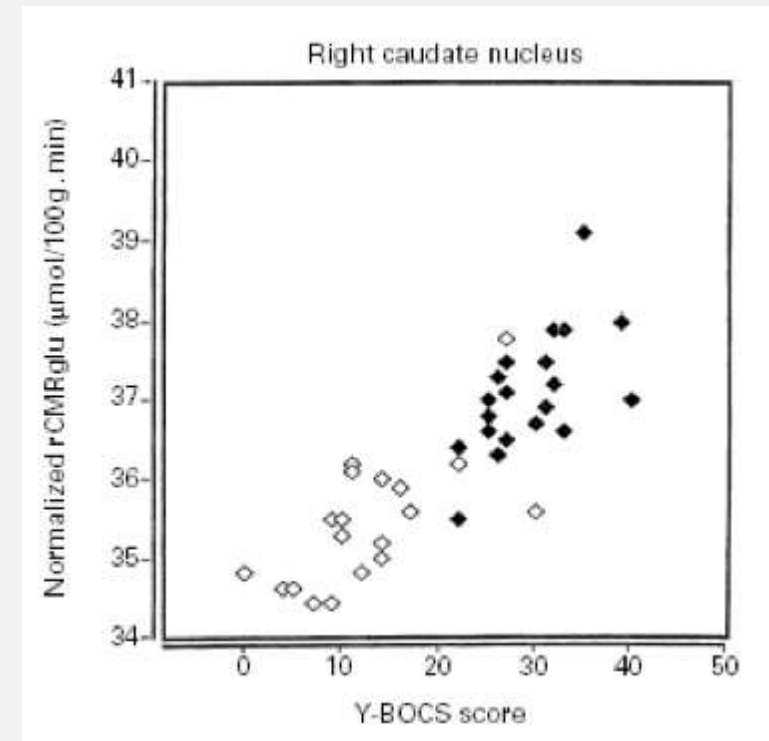
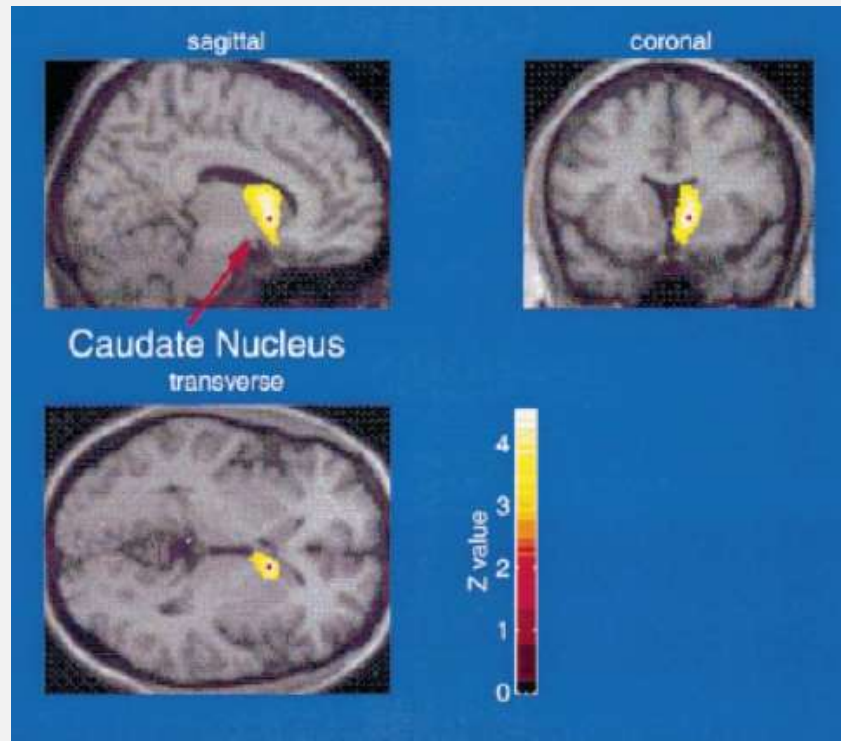


- 'Sensorimotor' CSTC circuit
 - Stimulus-response-based habitual behavior
- 'Dorsal cognitive' CSTC circuit
 - Working memory, planning and emotion regulation
- Frontoparietal network
 - Coordination of cognitive control
- 'Ventral cognitive' CSTC circuit
 - Response inhibition
- 'Ventral motivational' CSTC circuit
 - Stimulus-outcome-based motivational behaviour
- 'Frontolimbic' circuit
 - Fear extinction

PARALLEL CORTICO-STRIATAL CIRCUITS

Stein et al, 2019

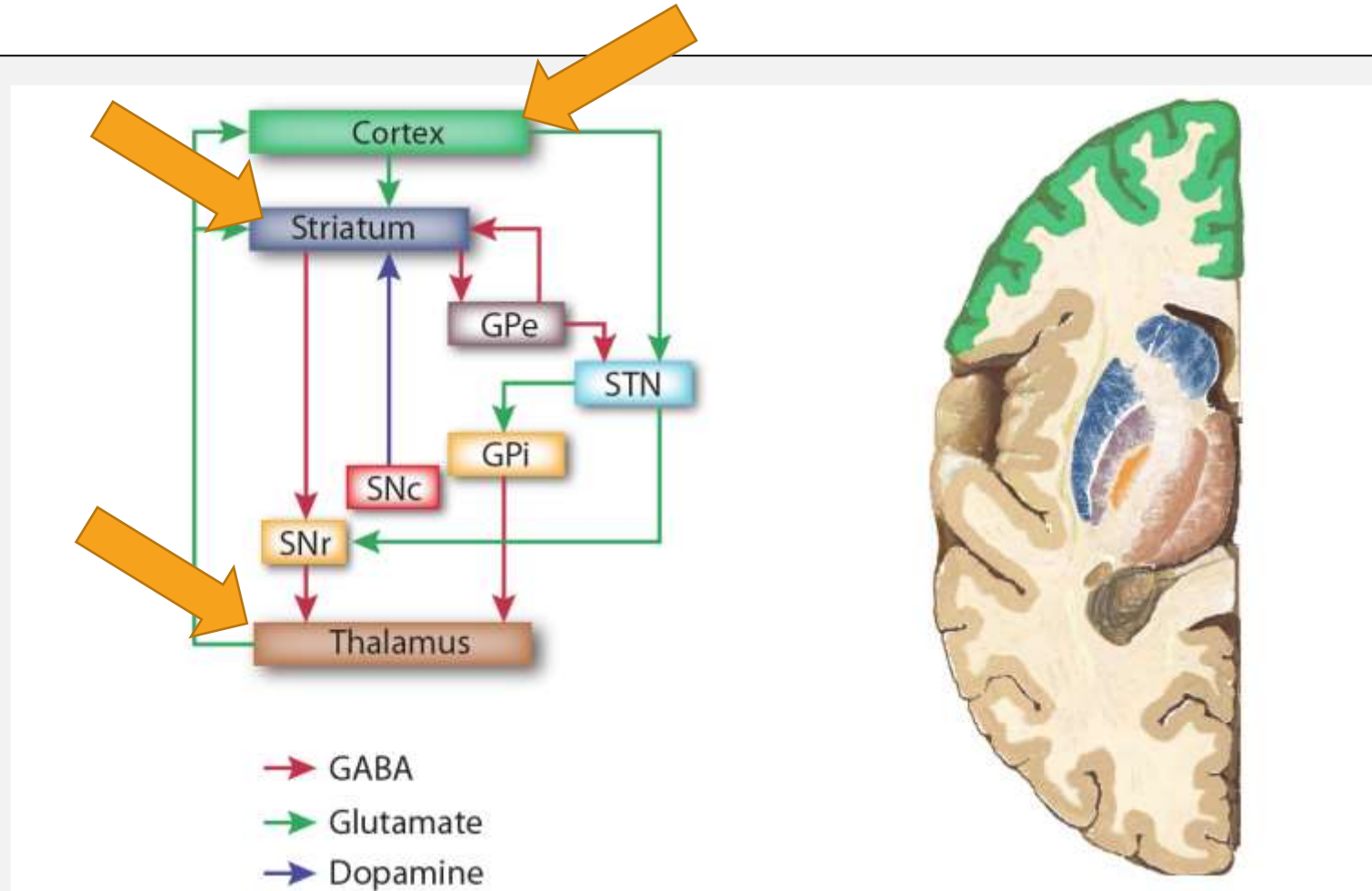
OBSESSIVE-COMPULSIVE DISORDER: NEURAL UNDERPINNINGS



EFFECT OF TREATMENT

Hansen et al, 2002

OBSESSIVE-COMPULSIVE DISORDER: NEURAL UNDERPINNINGS



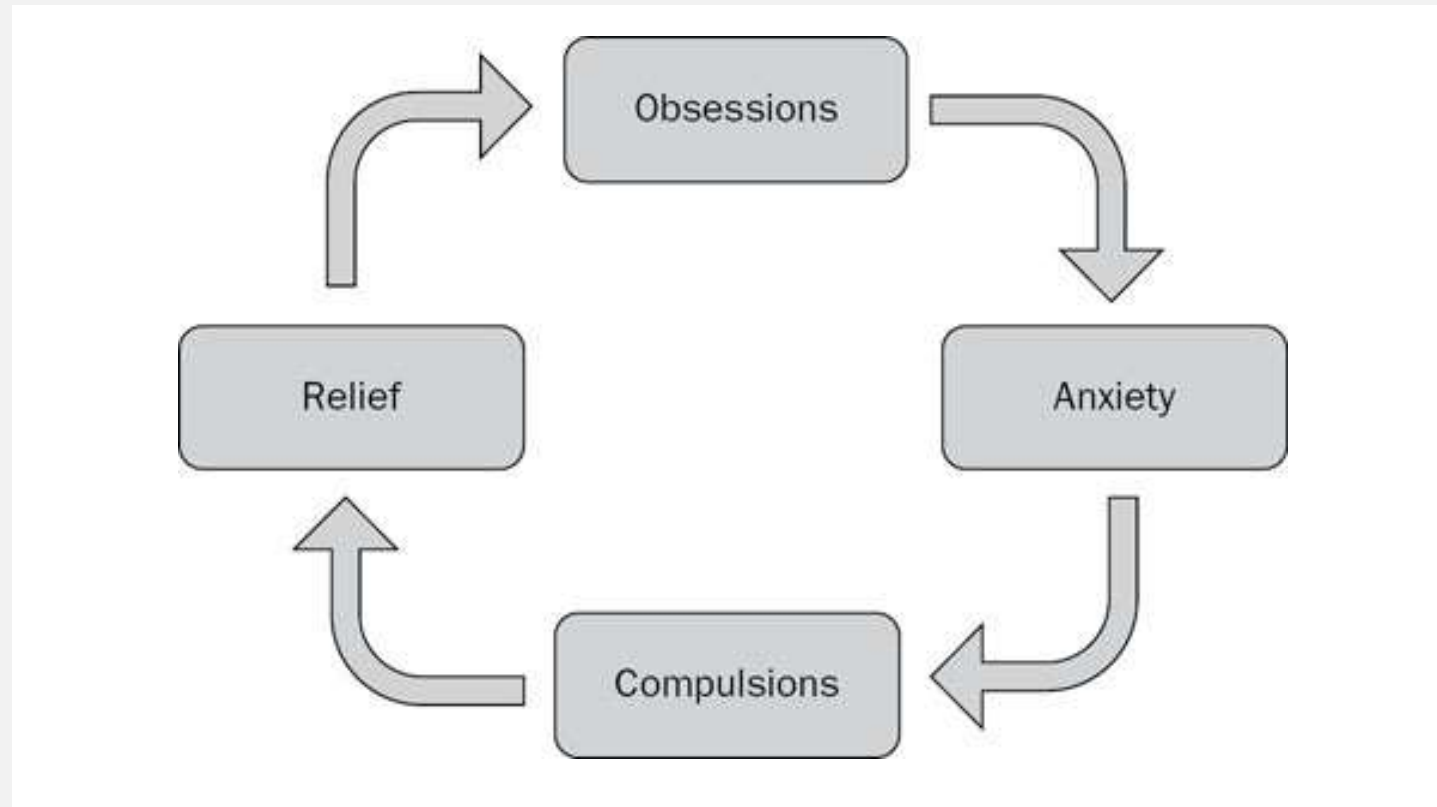
Pittenger et al, 2011

Van der Straten et al, 2017

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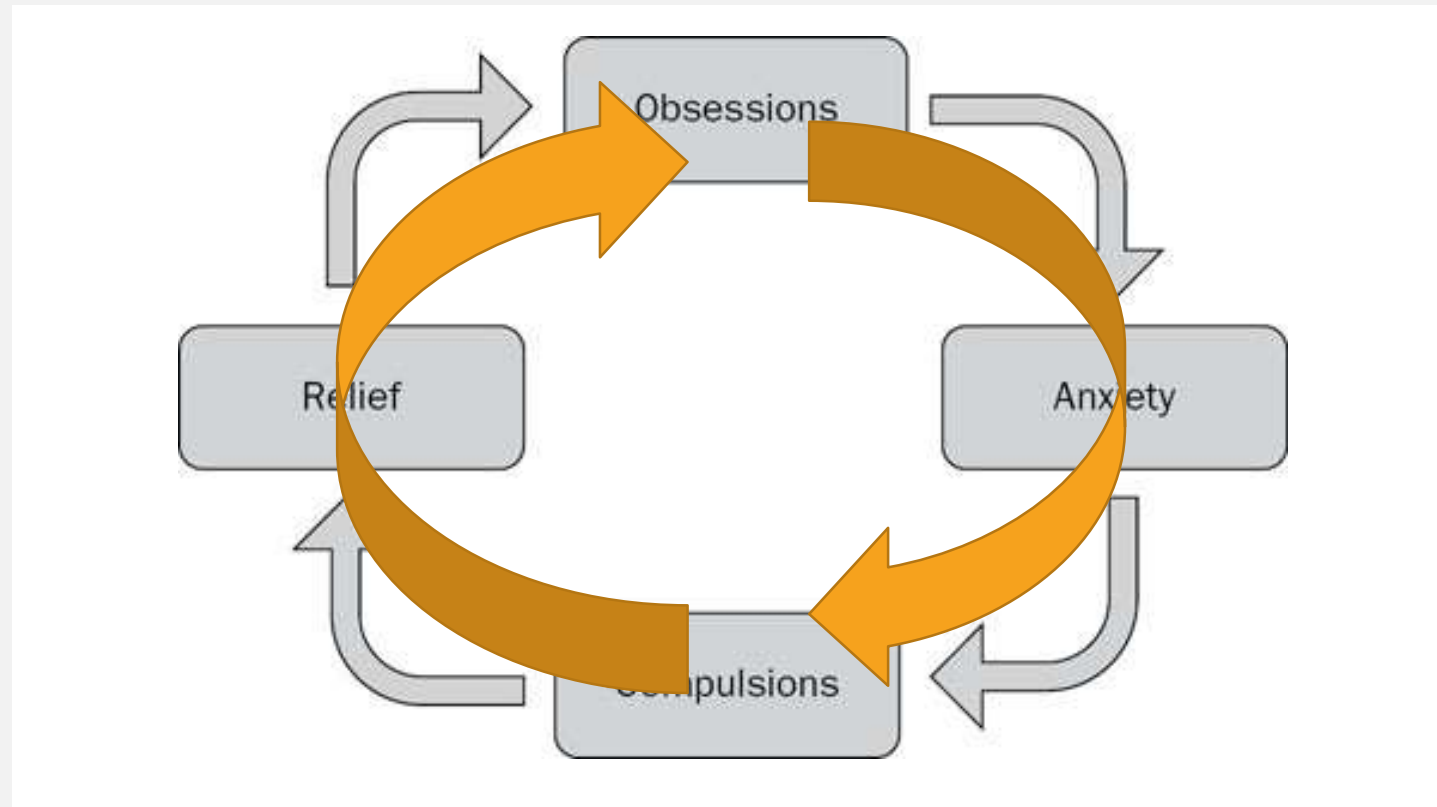
A FRAMEWORK FOR UNDERSTANDING OBSESSIONS AND COMPULSIONS



A CLASSICAL VIEW

Pittenger et al, 2017

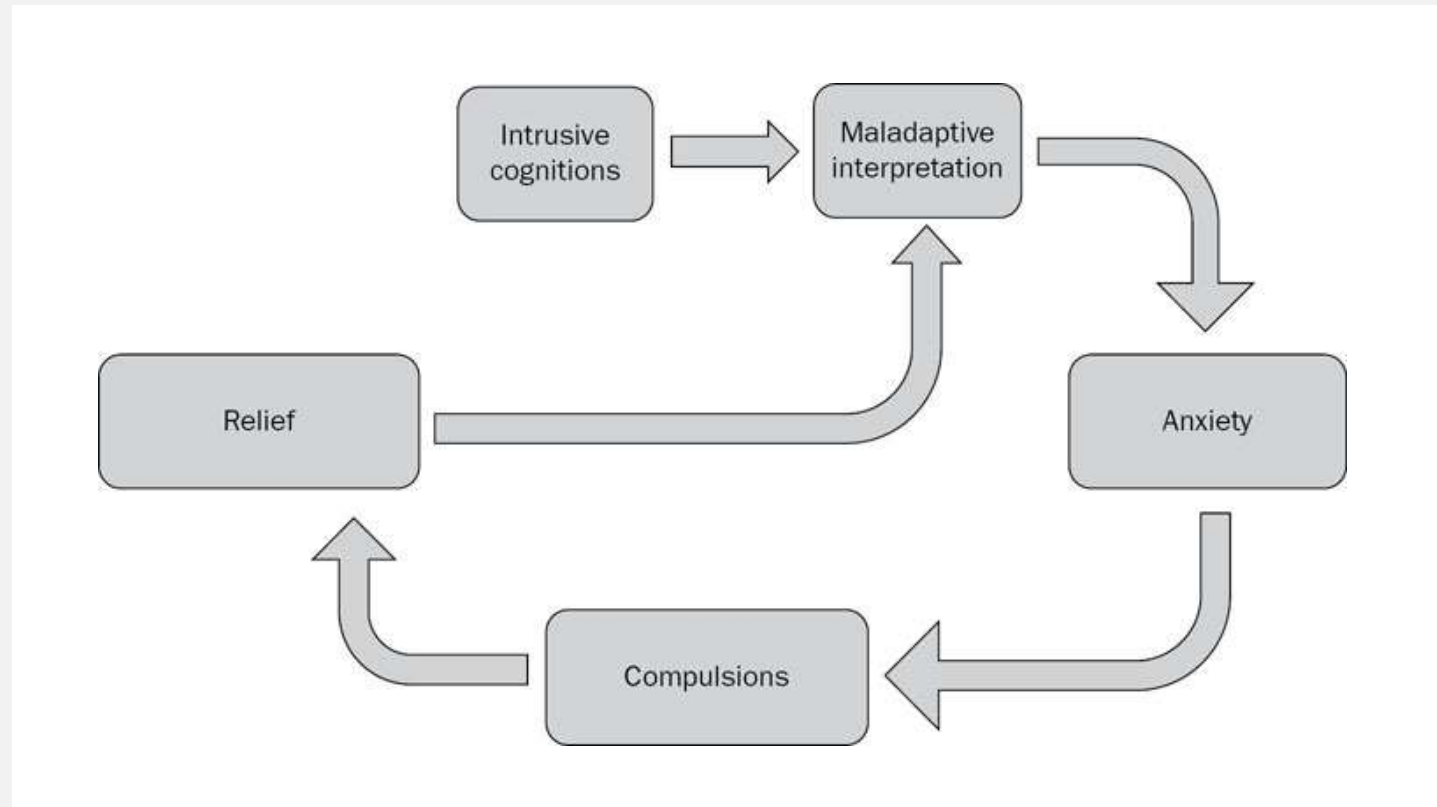
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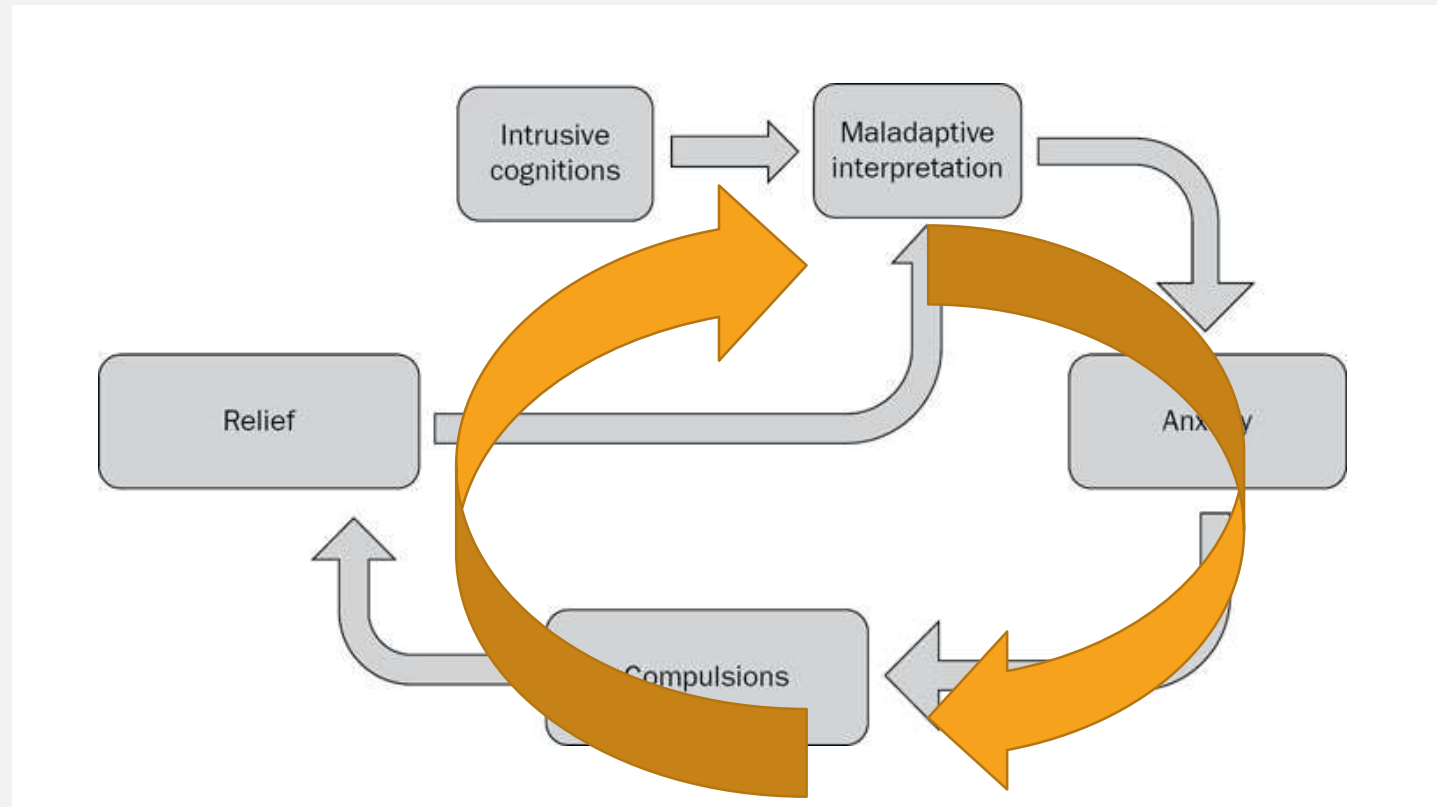
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AN UPDATED VIEW

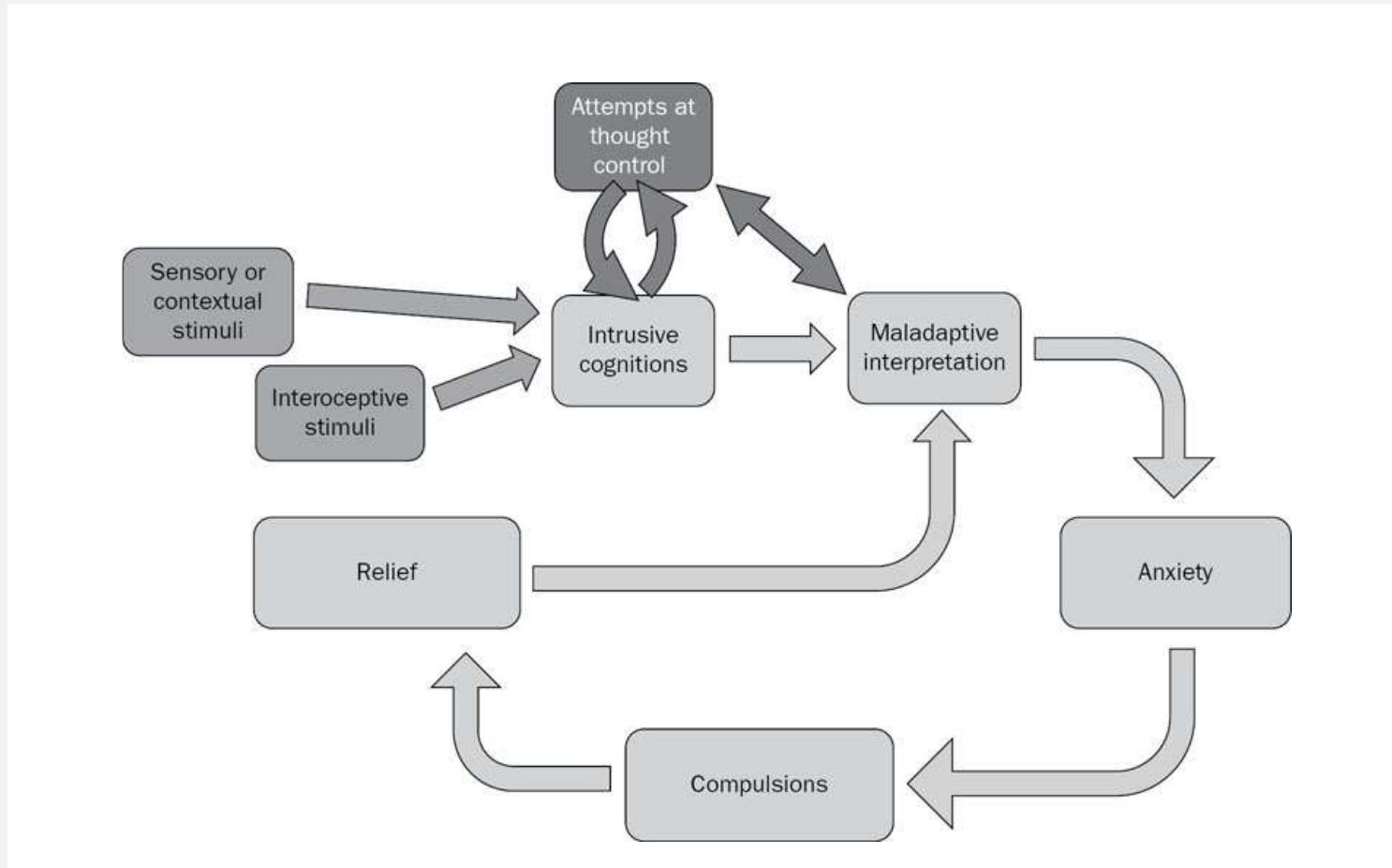
Pittenger et al, 2017

A FRAMEWORK FOR UNDERSTANDING OBSESSIONS AND COMPULSIONS



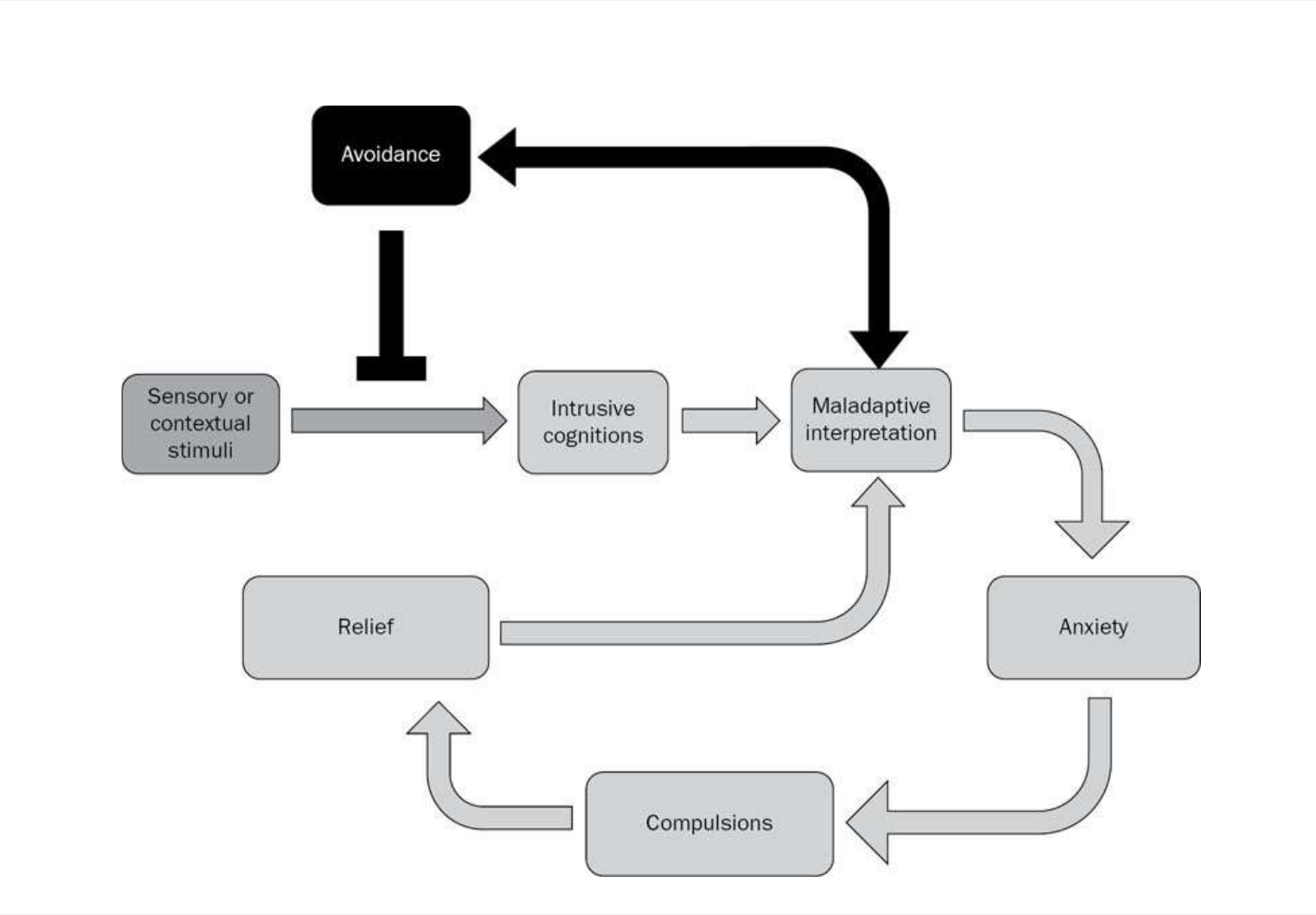
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Pittenger et al, 2017



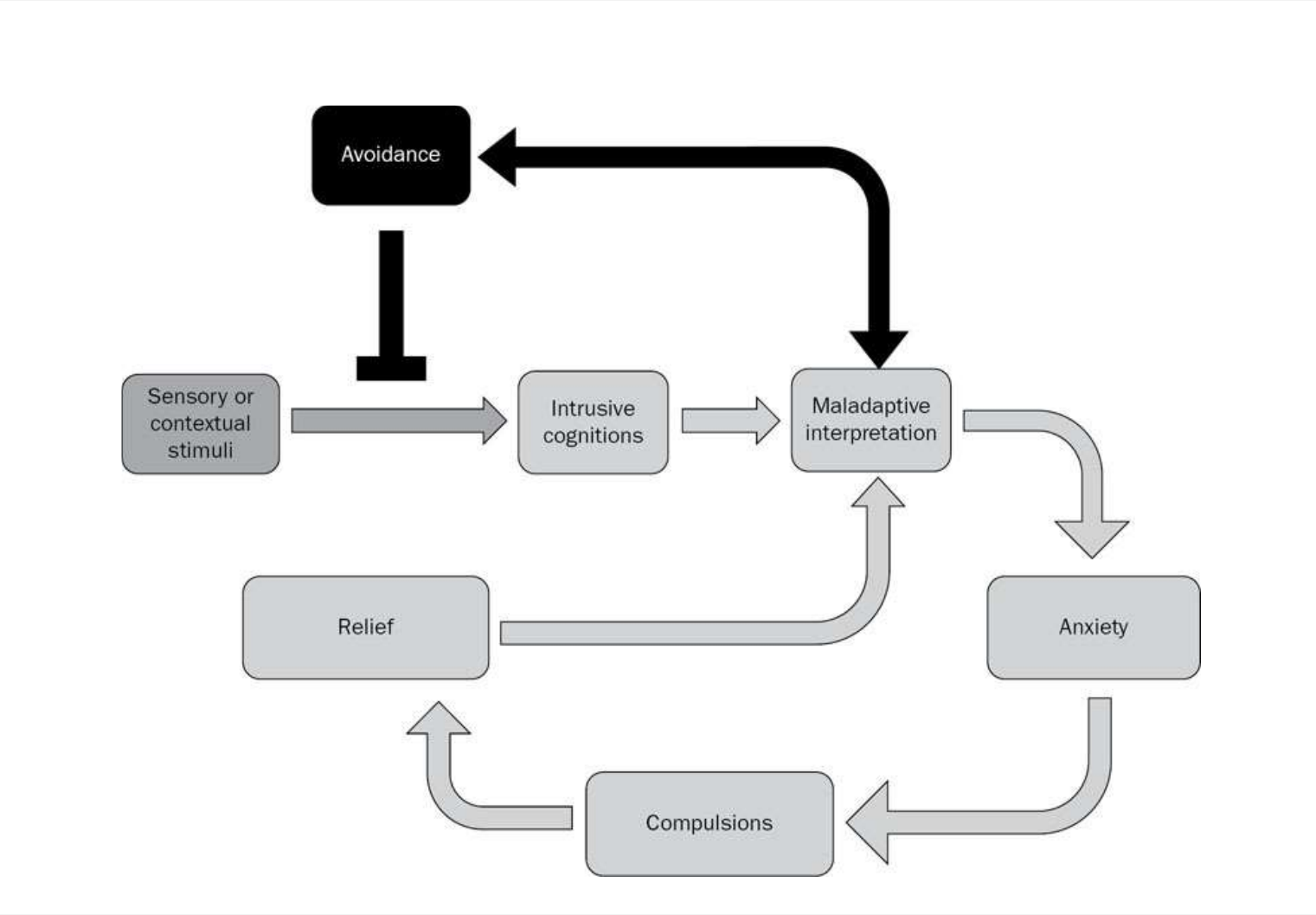
TRIGGERS

Pittenger et al, 2017



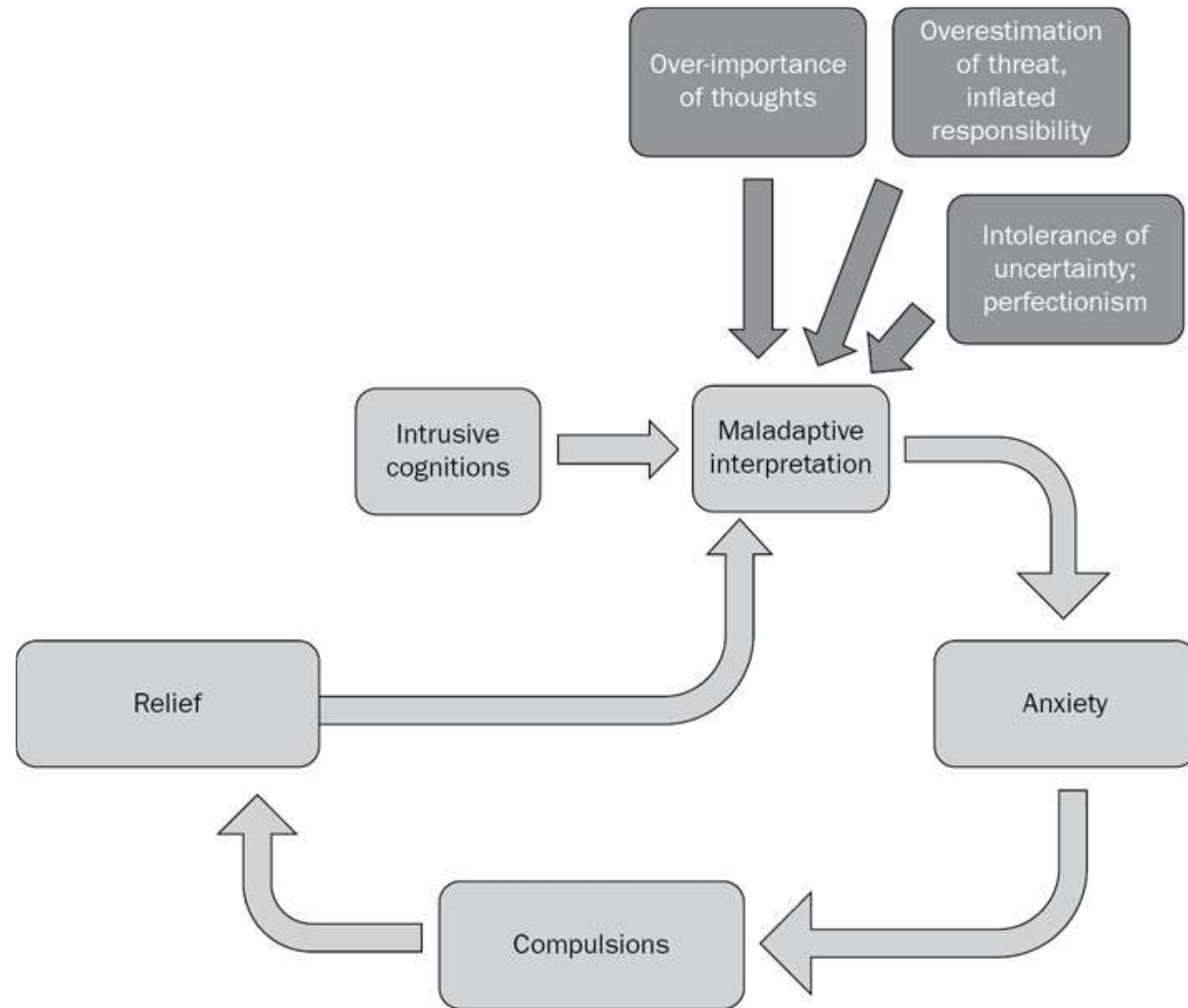
AVOIDANCE

Pittenger et al, 2017



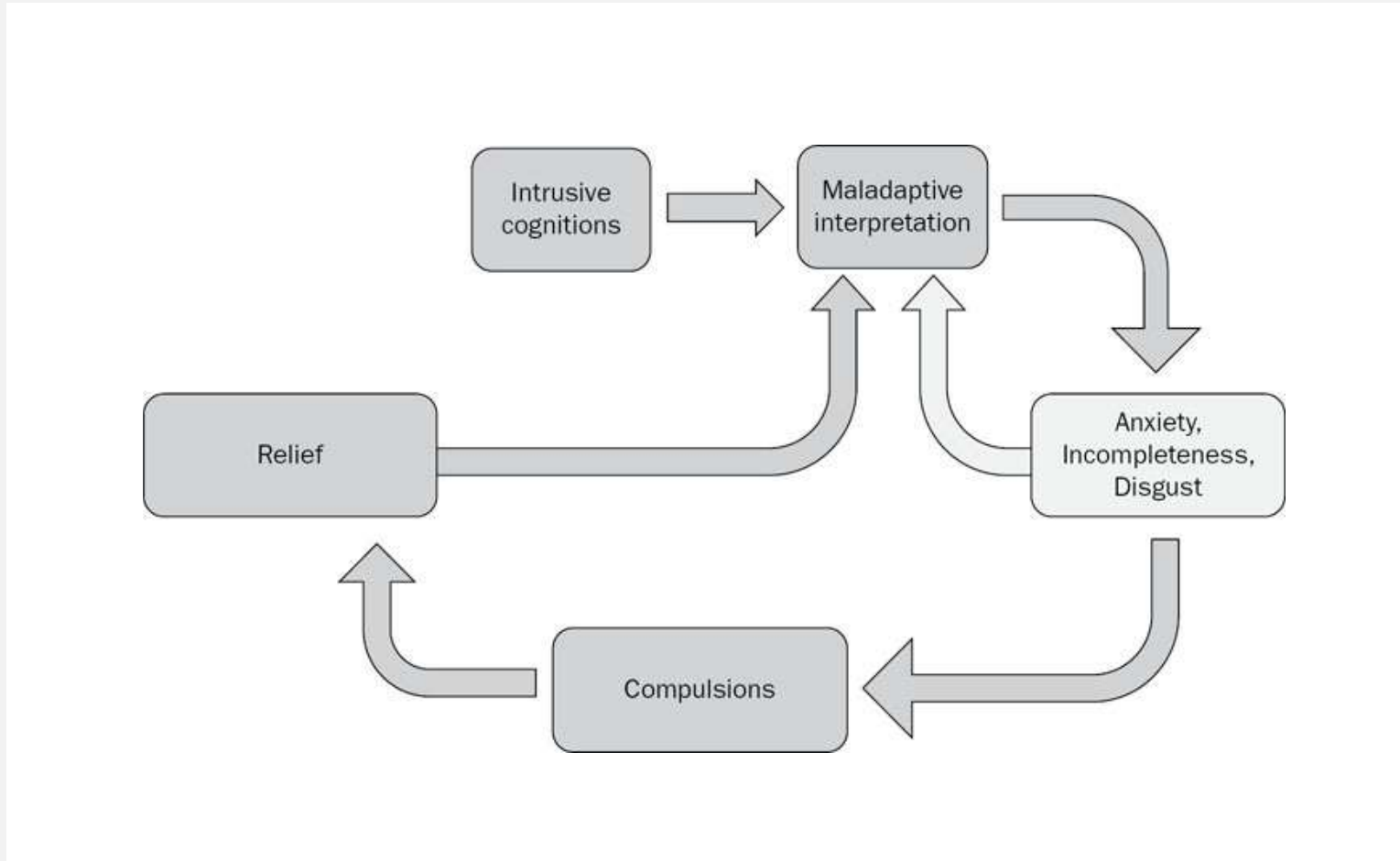
AVOIDANCE

Pittenger et al, 2017



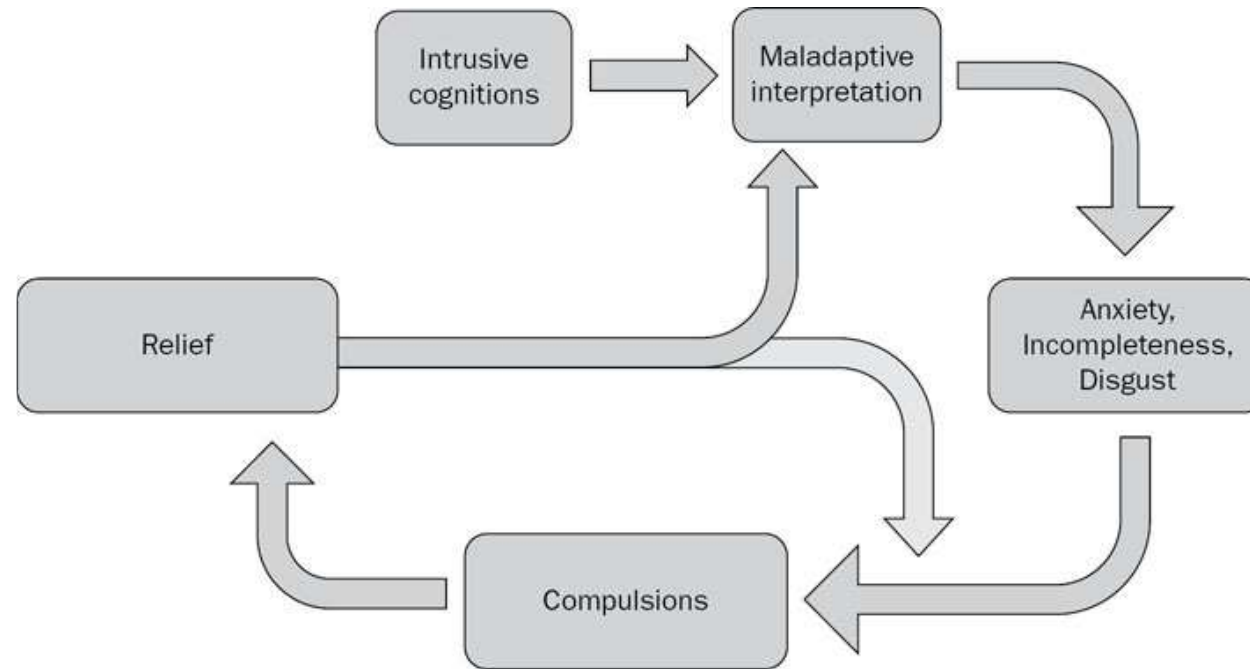
COGNITIVE BIASES AND DISTORTIONS

Pittenger et al, 2017



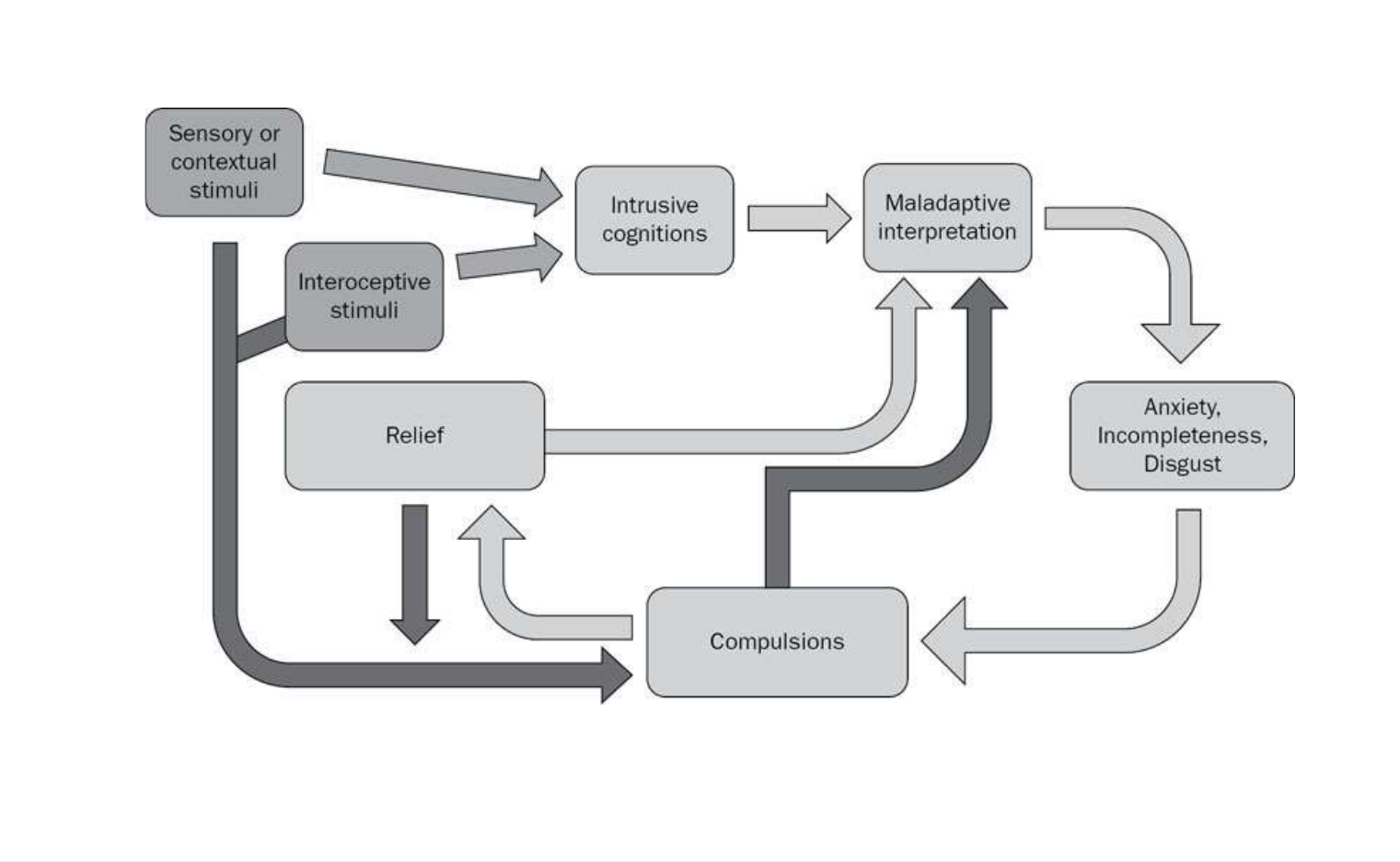
THE ROLE OF AFFECT

Pittenger et al, 2017



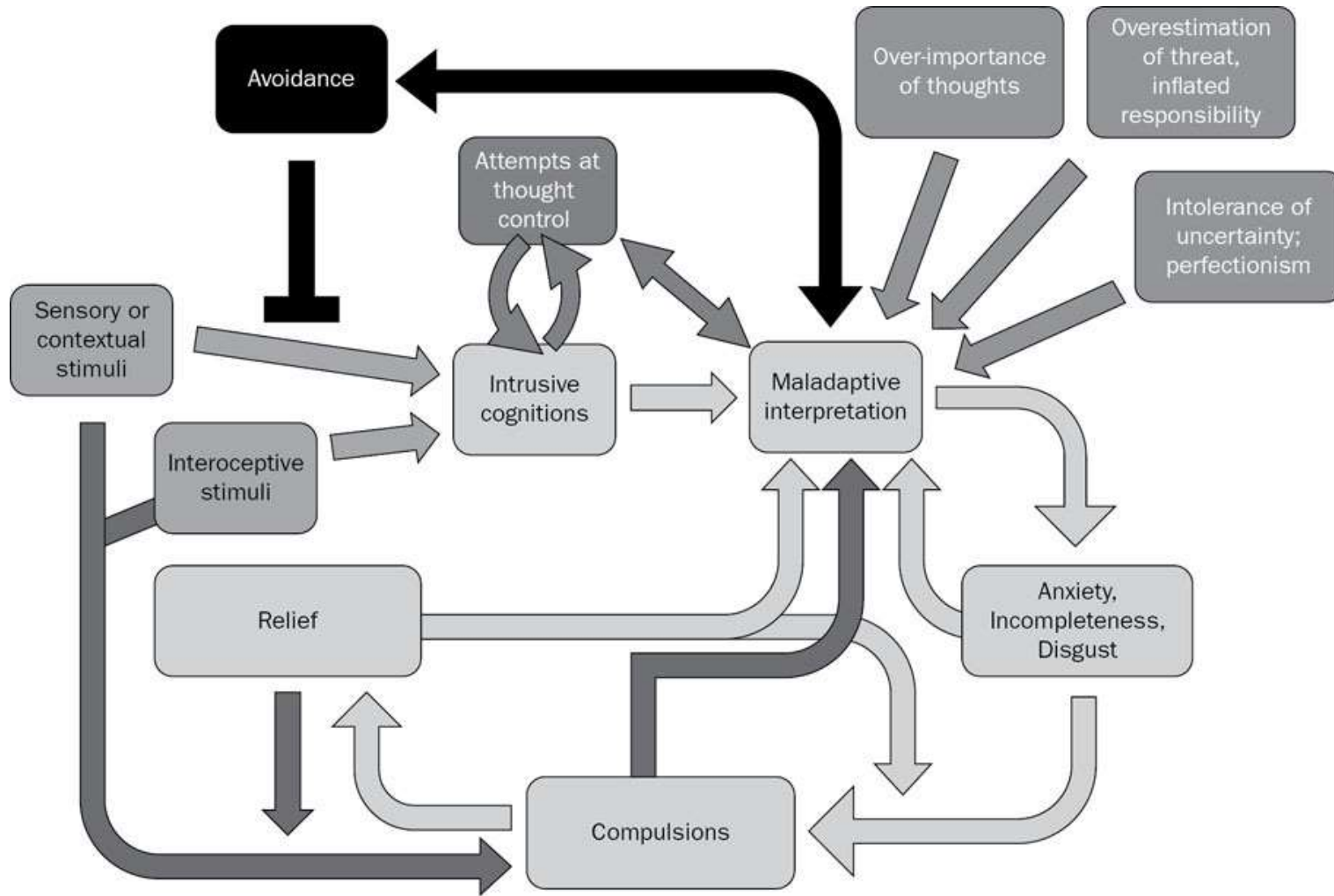
DIRECT REINFORCEMENT OF COMPULSIONS

Pittenger et al, 2017



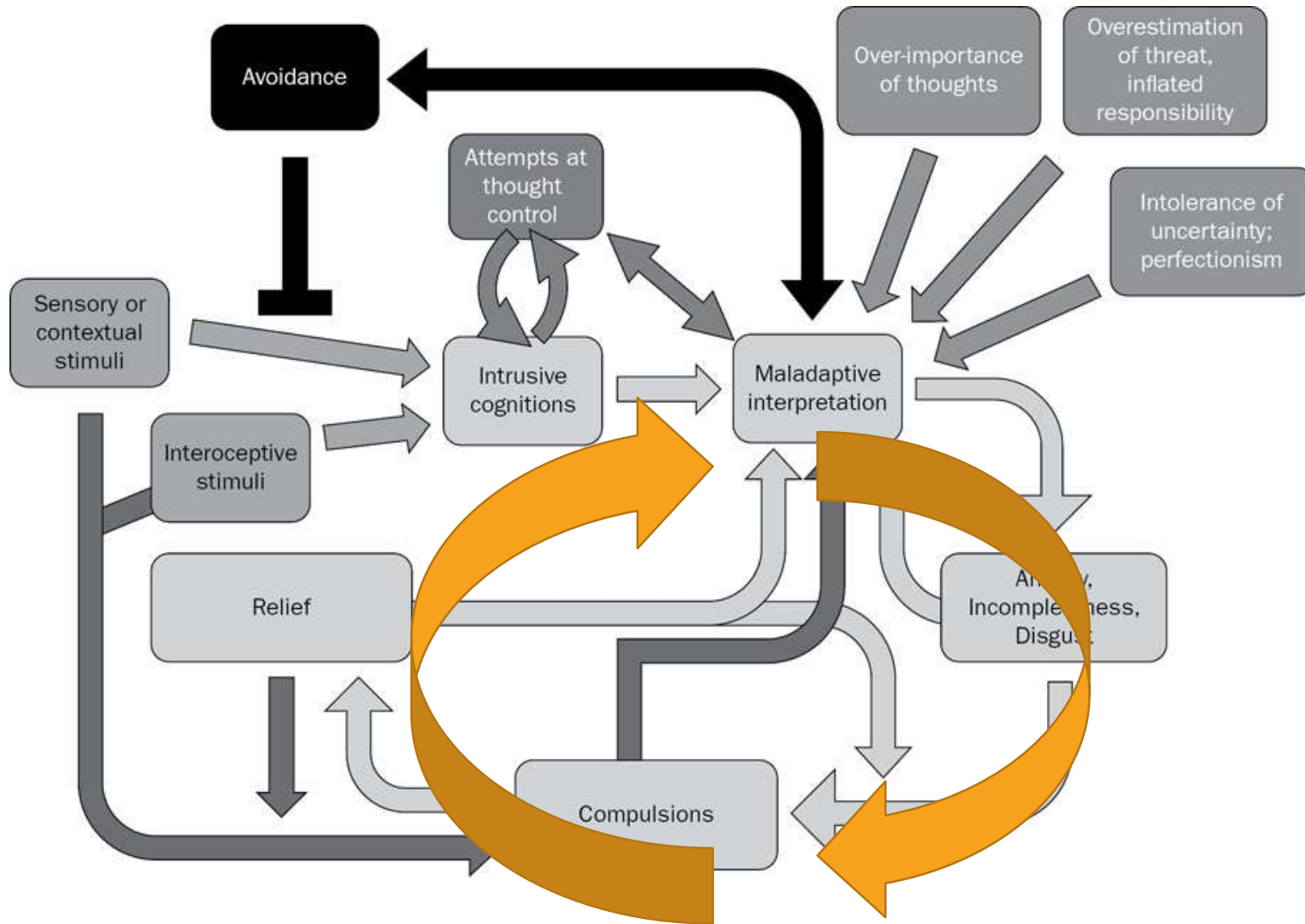
DEVELOPMENT OF HABITS

Pittenger et al, 2017



PUTTING IT ALL TOGETHER

Pittenger et al, 2017



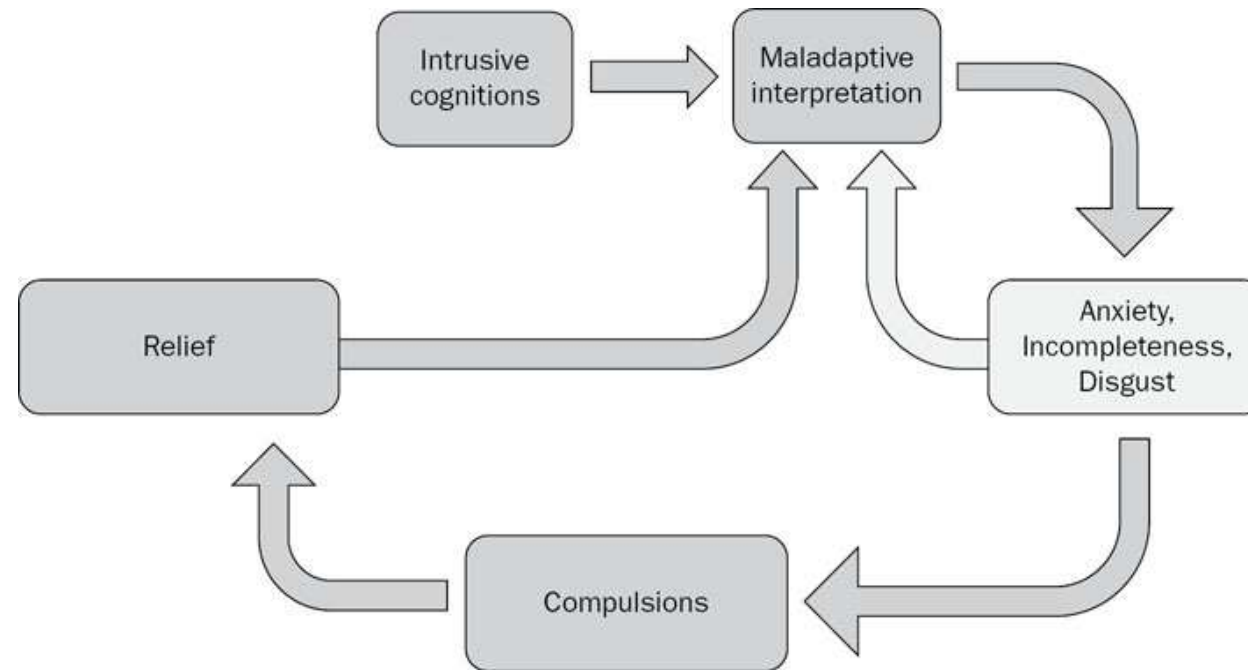
PUTTING IT ALL TOGETHER

Pittenger et al, 2017

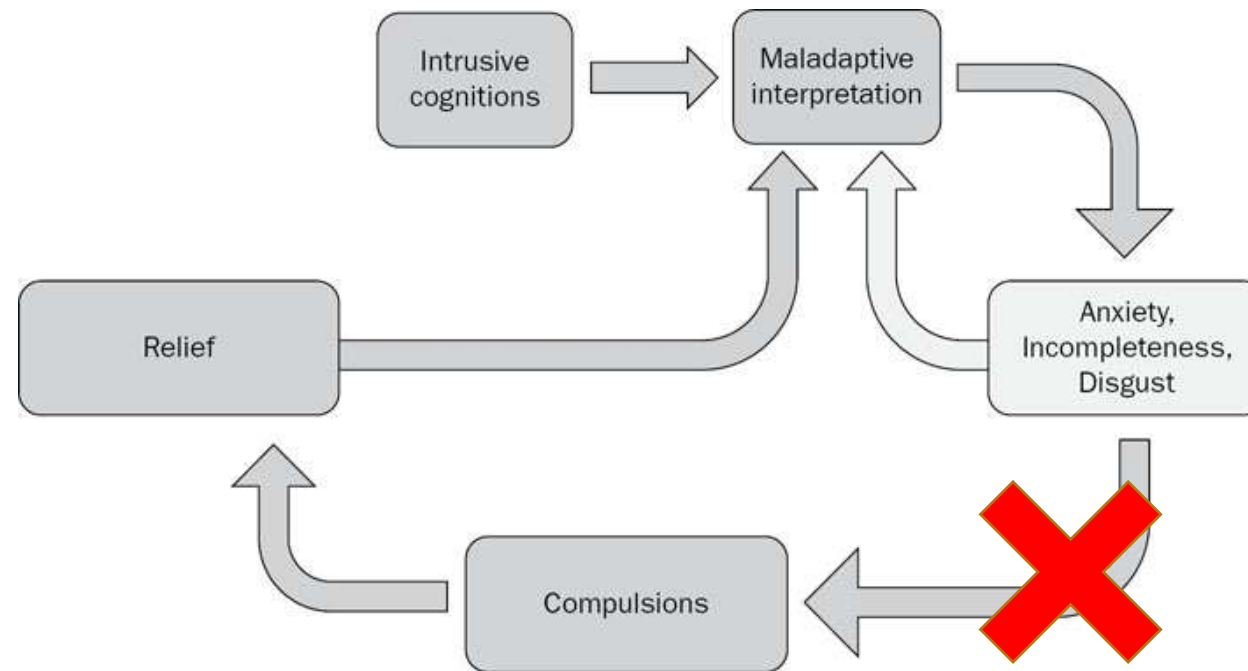
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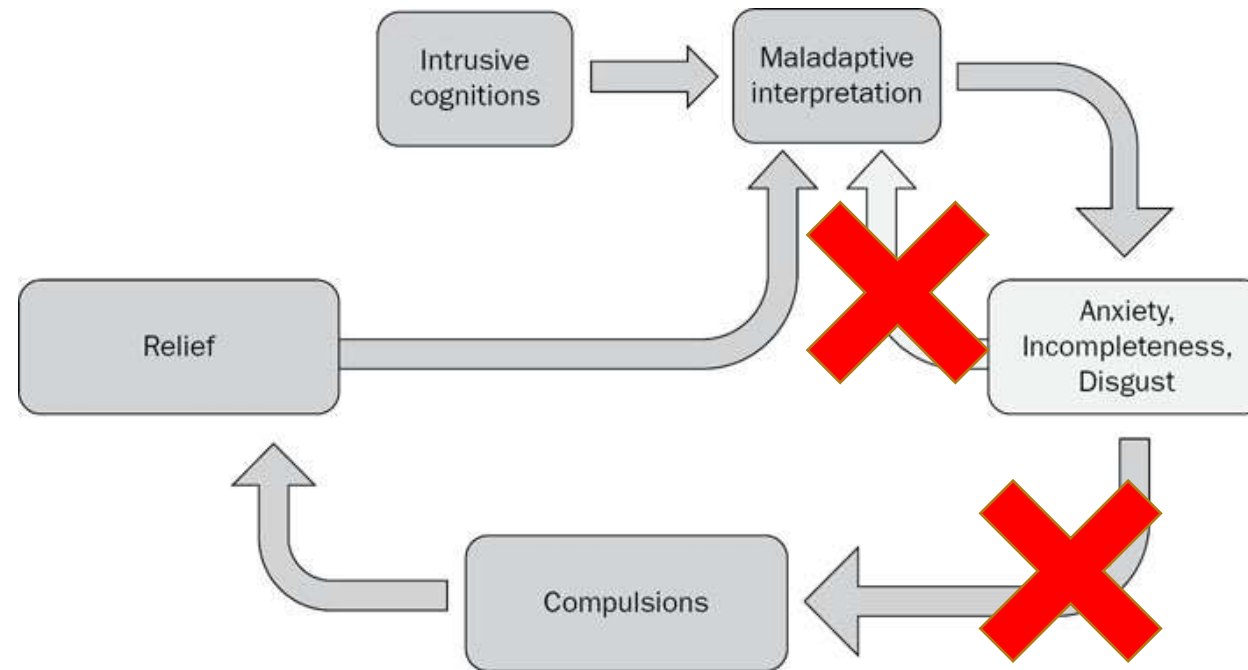
PSYCHOTHERAPY SEEKS TO INTERRUPT THE FEEDBACK CYCLE



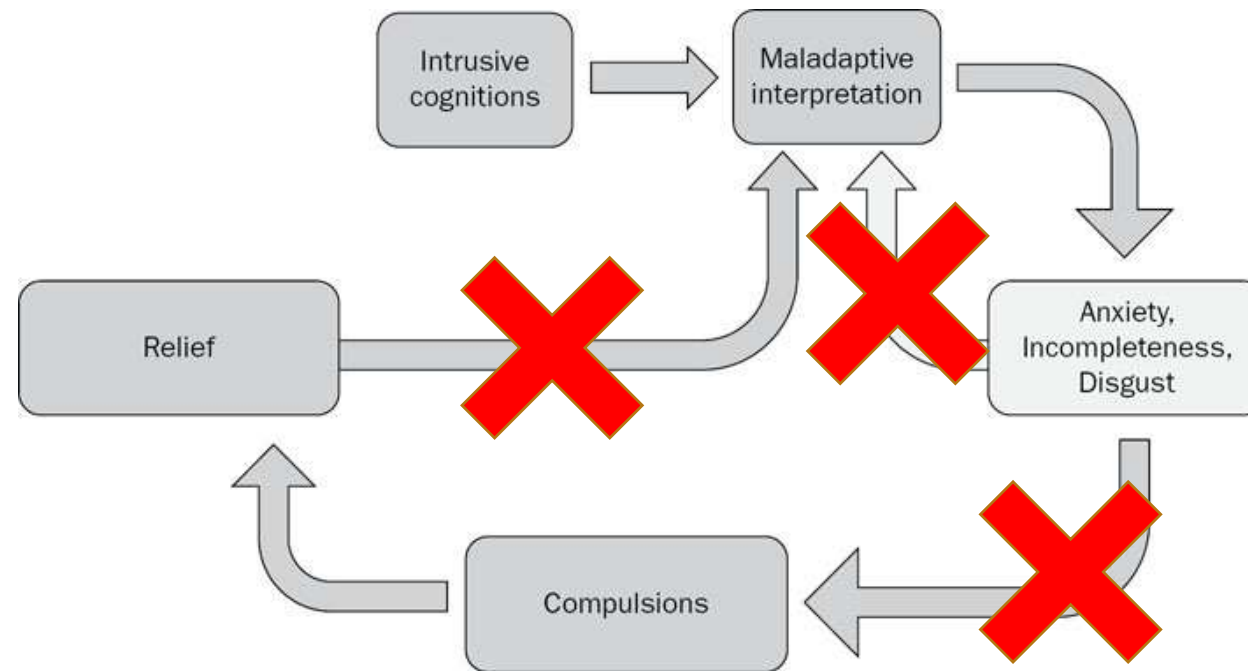
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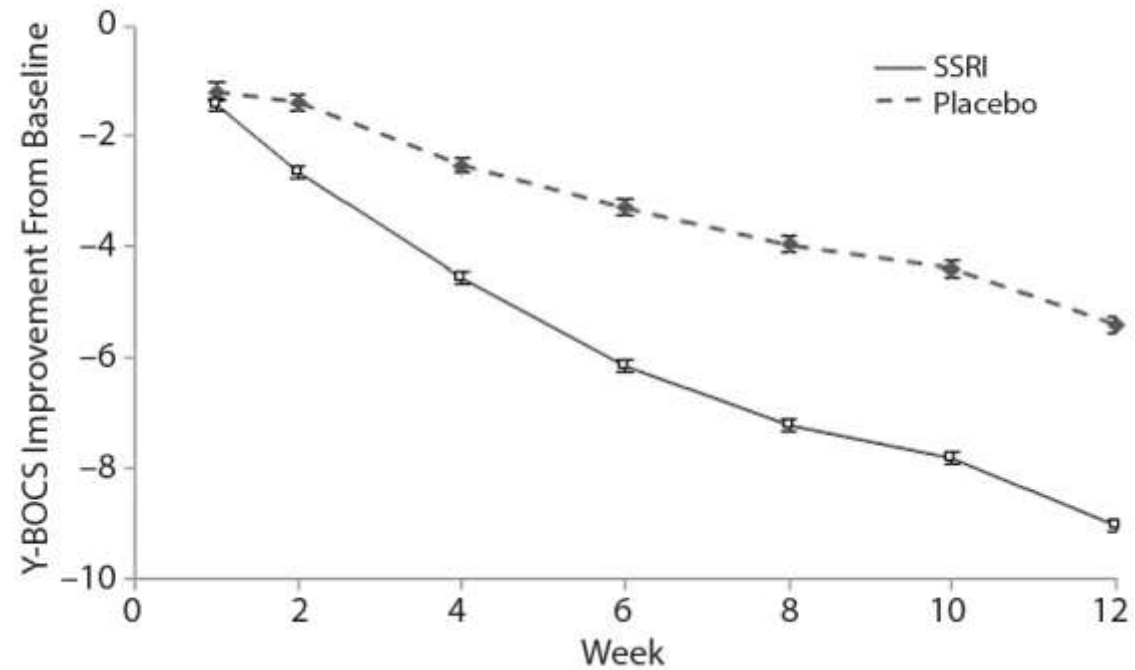
SEROTONIN REUPTAKE INHIBITORS: FIRST LINE PHARMACOLOGICAL TREATMENT

- Fluoxetine (Prozac)
- Fluvoxamine (Luvox)
- Sertraline (Zoloft)
- Paroxetine (Paxil)
- Citalopram (Celexa)
- Escitalopram (Lexapro)
- Clomipramine (Anafranil)*

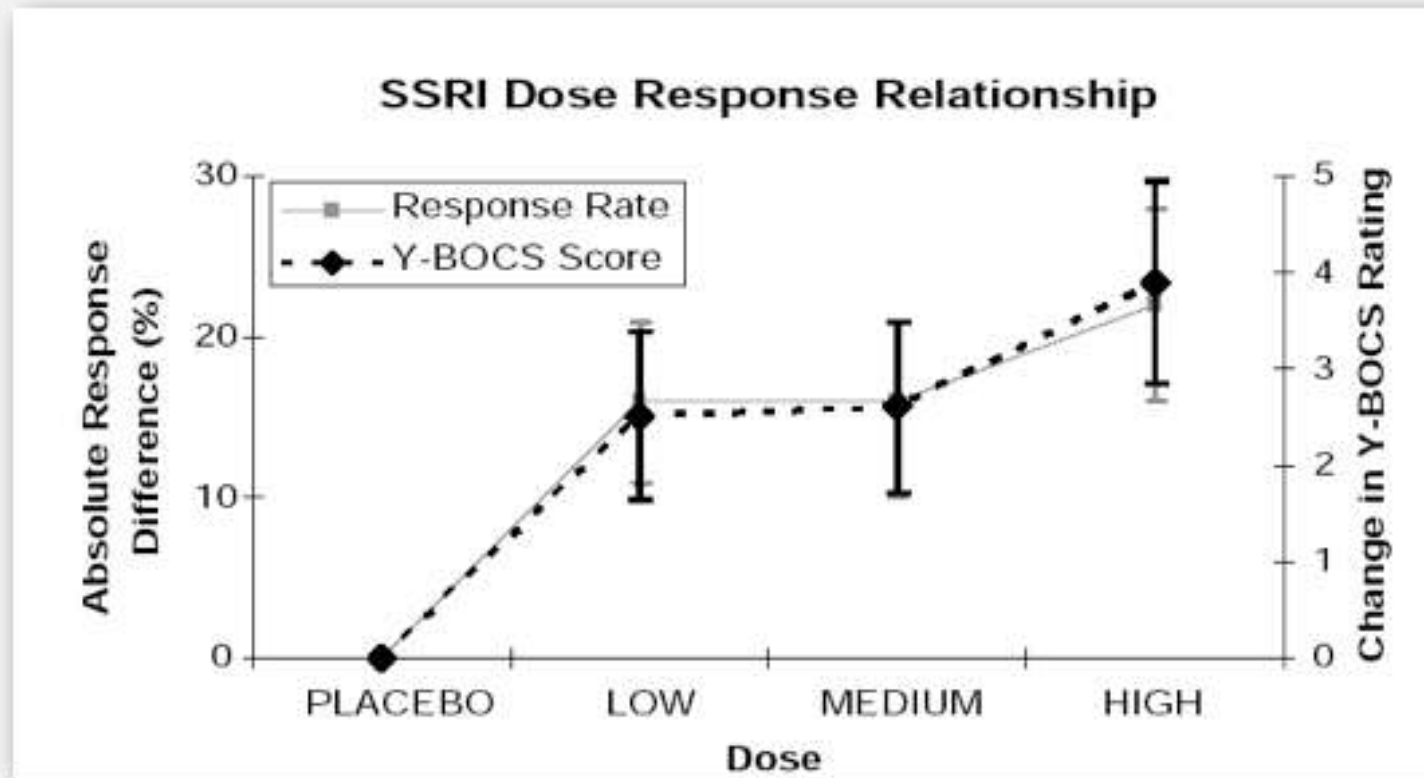


SEROTONIN REUPTAKE INHIBITORS

C. Change from Baseline in Y-BOCS for SSRI and Placebo^a



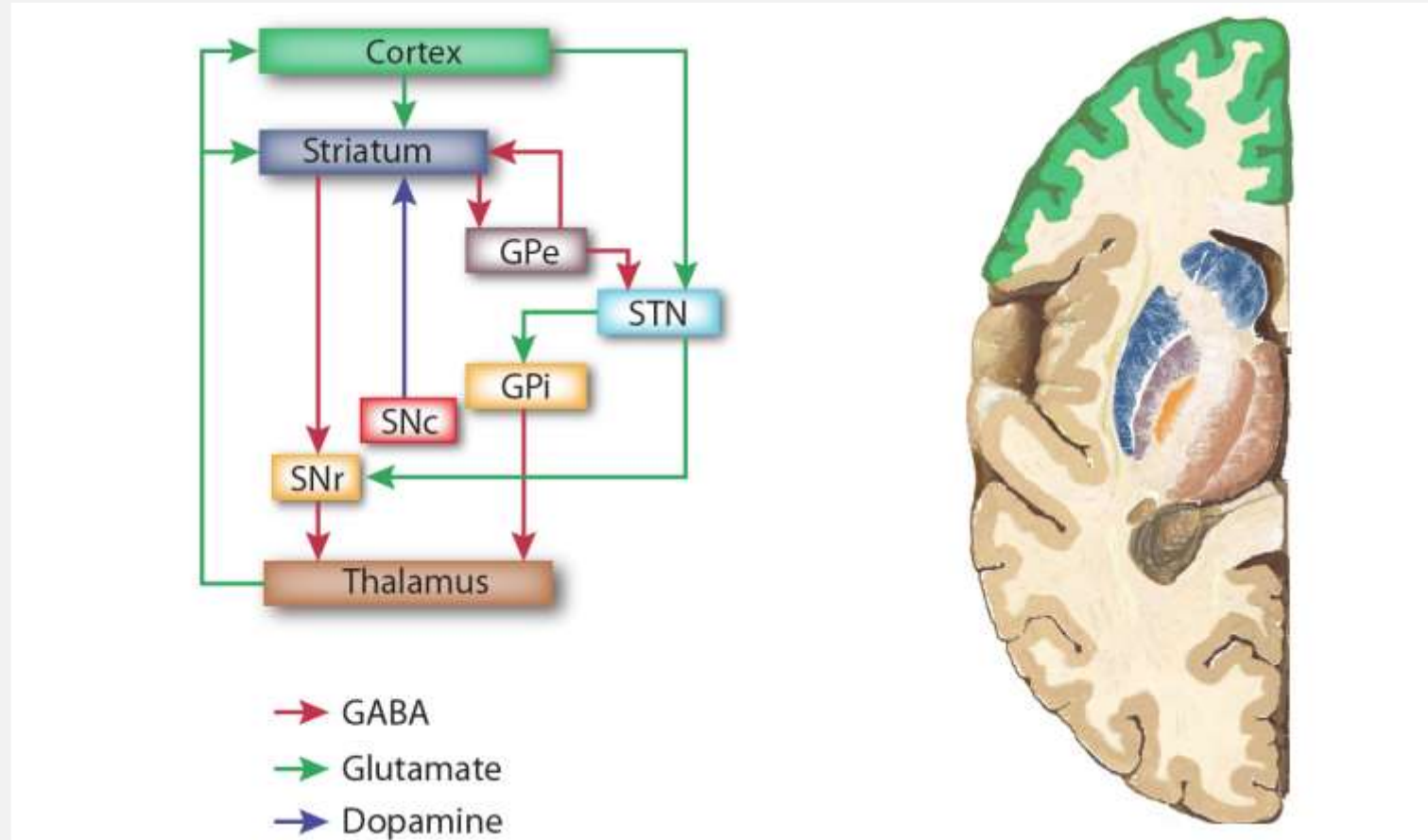
SEROTONIN REUPTAKE INHIBITORS



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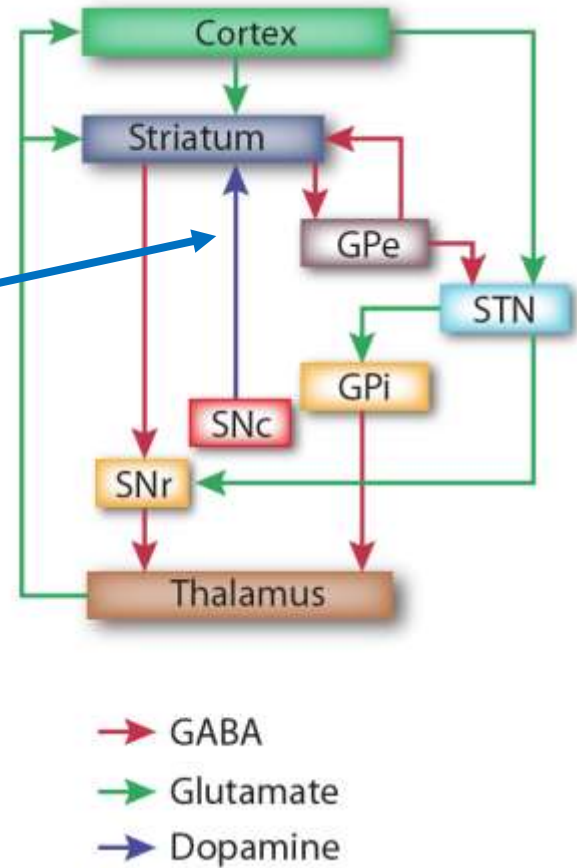
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OTHER PHARMACOLOGICAL TARGETS?



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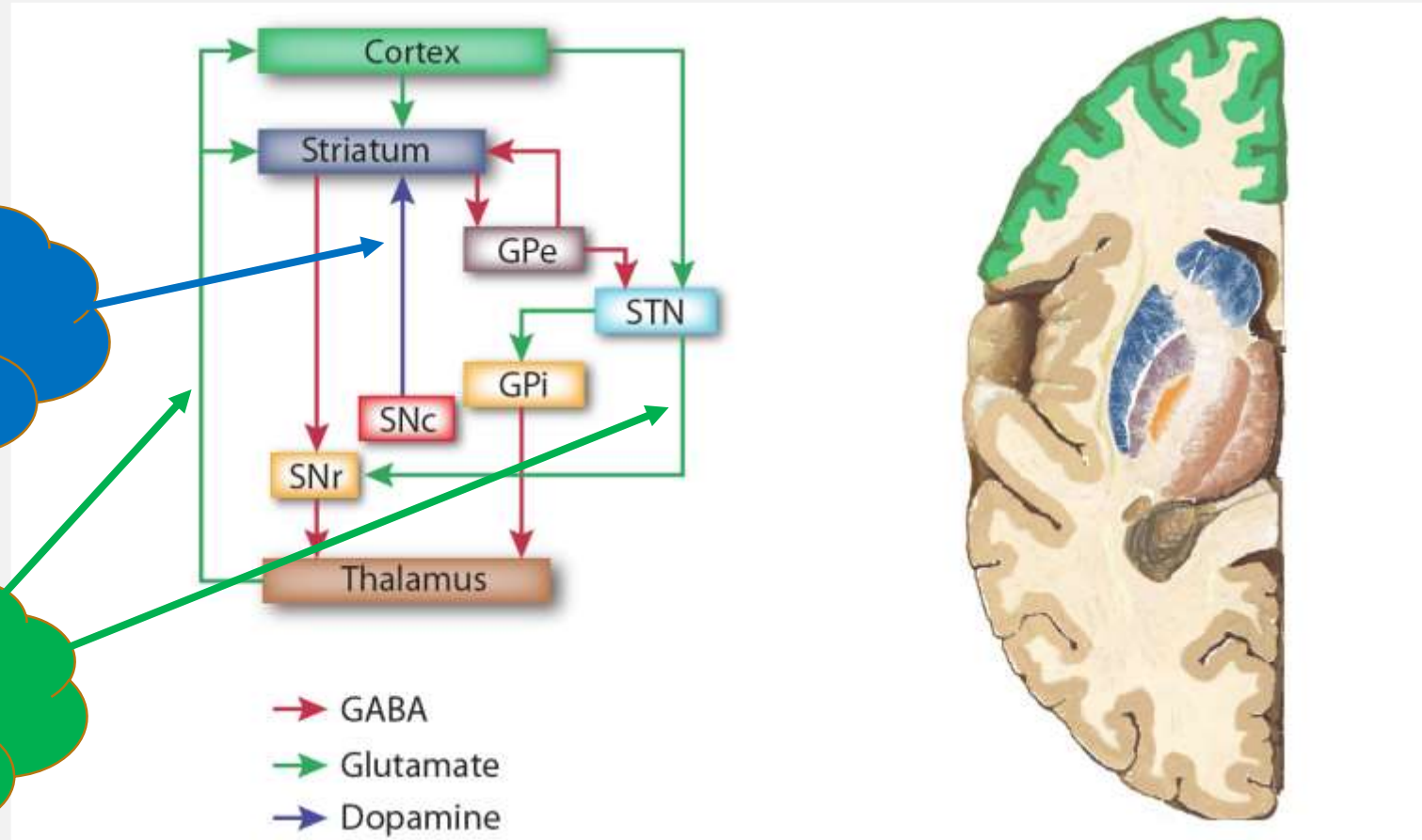
Dopamine



OTHER PHARMACOLOGICAL TARGETS?

Dopamine

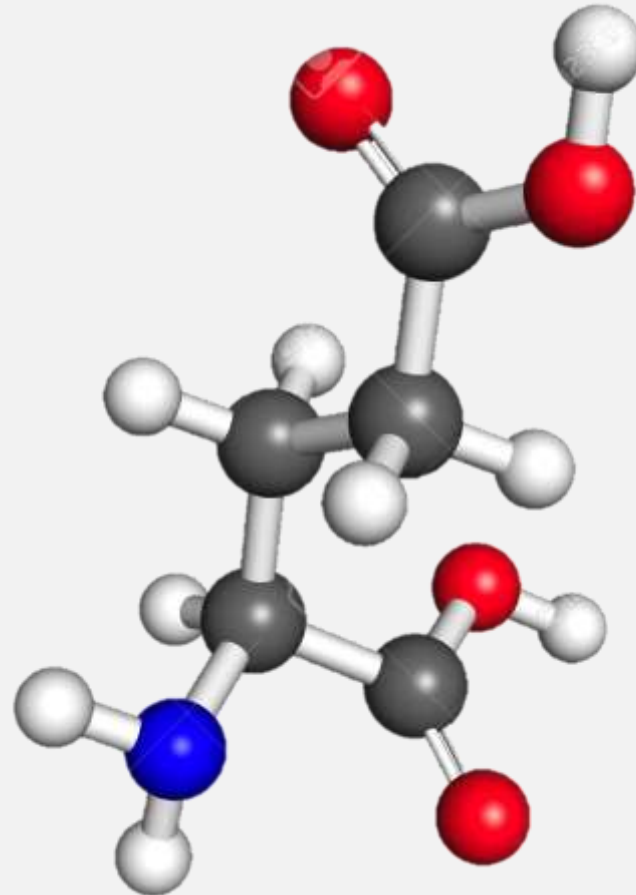
Glutamate



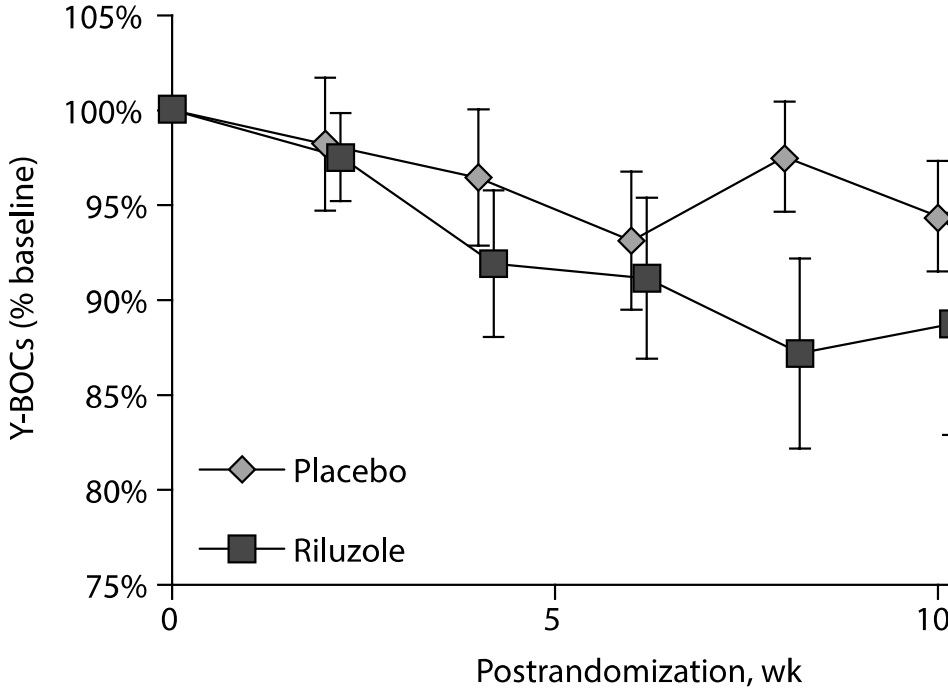
GLUTAMATE MODULATORS

- Riluzole (Rilutek)
- Memantine (Namenda)
- Ketamine

Glutamate modulators in OCD remains investigational; better-proven agents should always be tried first!

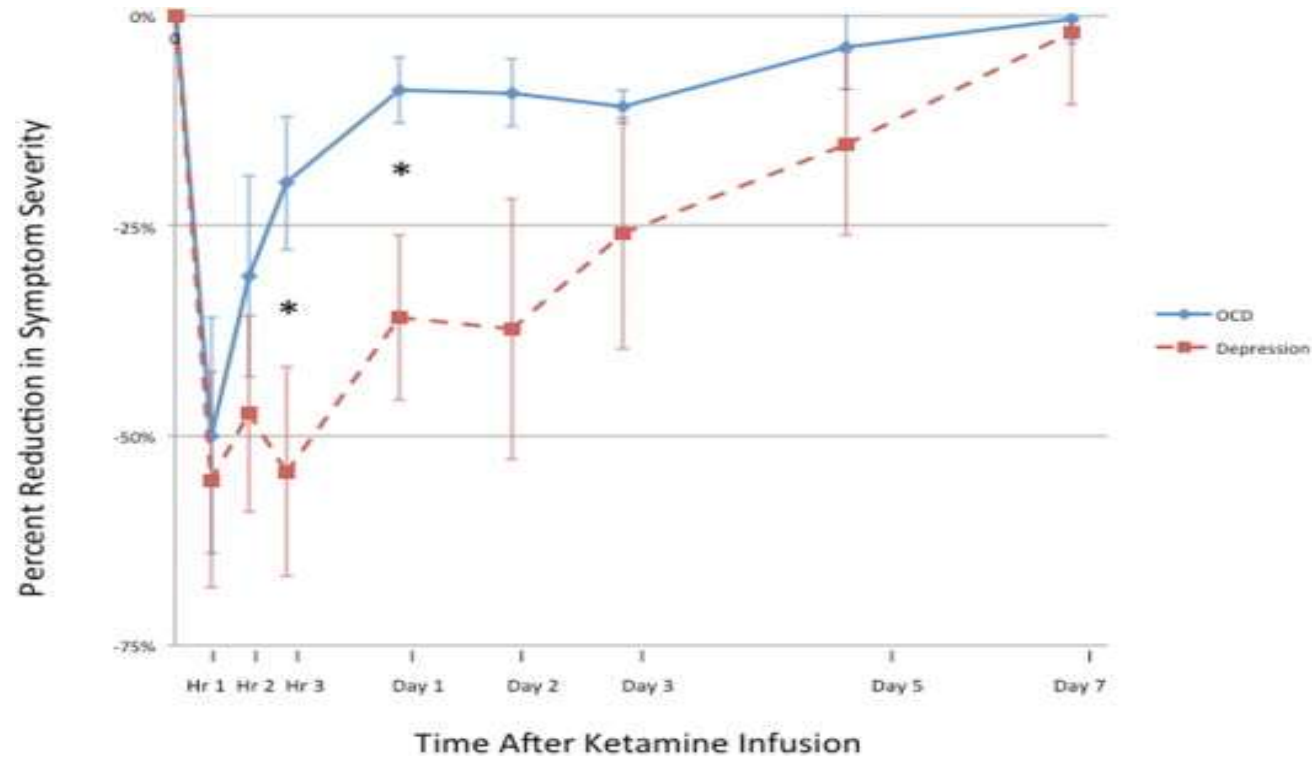


RILUZOLE



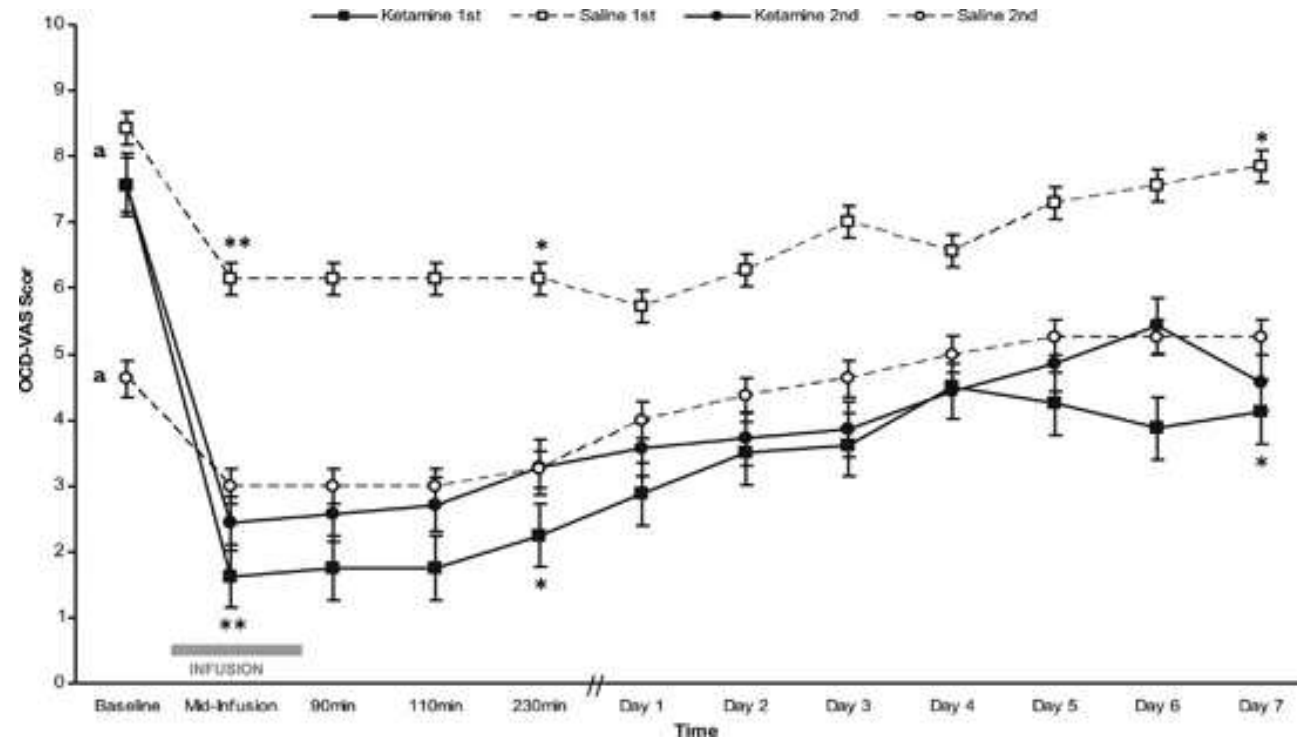
Pittenger et al, 2015

KETAMINE



Bloch et al, 2012

KETAMINE

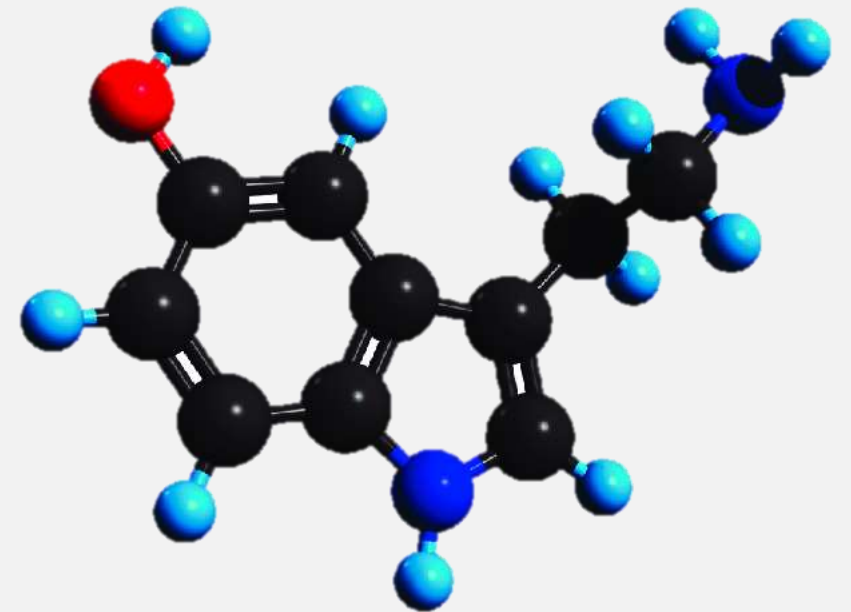


Rodriguez et al, 2013

OTHER SEROTONIN MODULATORS

- Mirtazapine (Remeron)
- Bupropion (Wellbutrin)
- Psilocybin

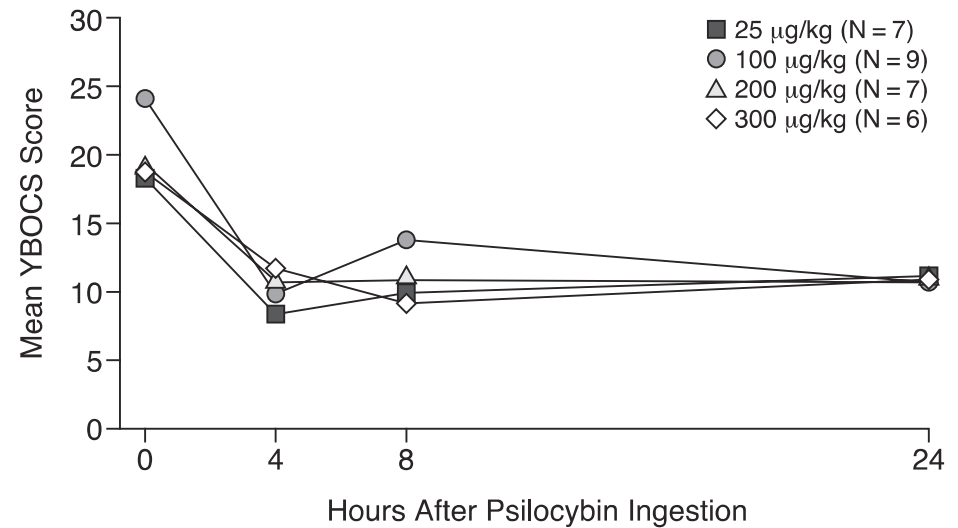
These agents remain investigational in OCD; better-proven agents should always be tried first!



PSILOCYBIN??!?



Figure 1. Effects of Psilocybin on Obsessive-Compulsive Symptom Severity^a

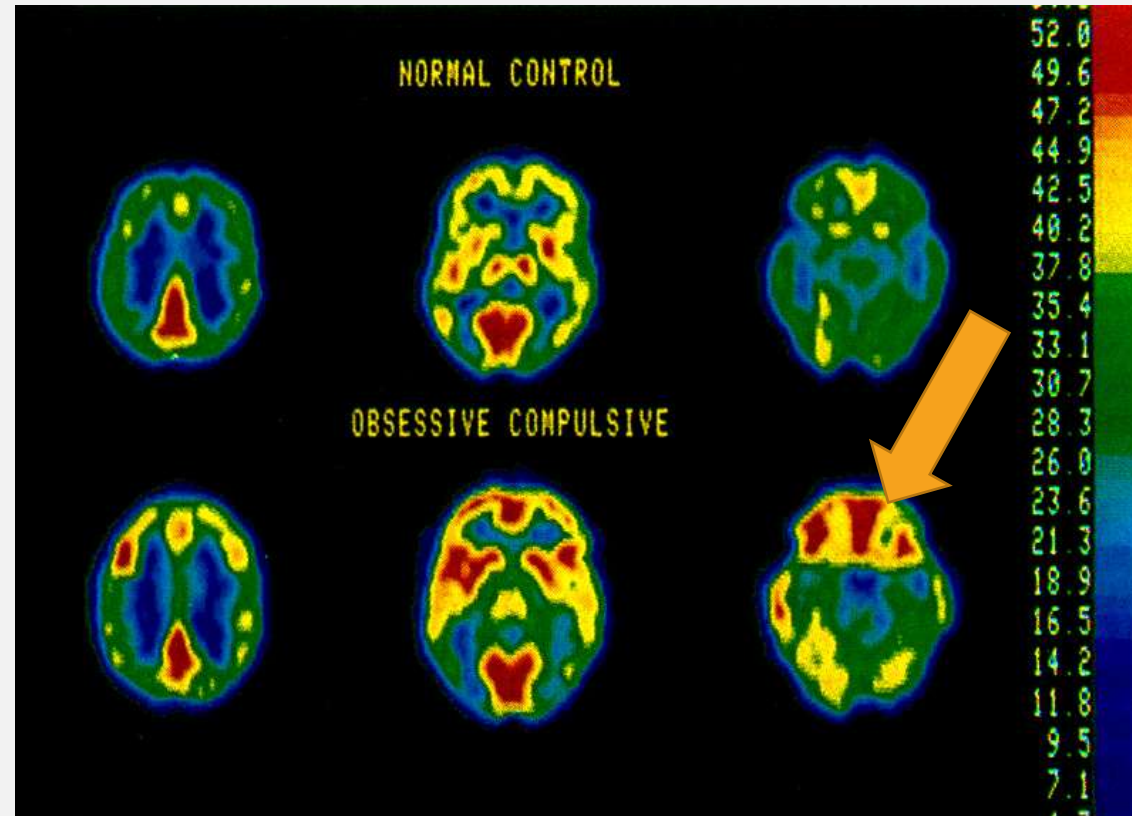


Moreno et al, 2006

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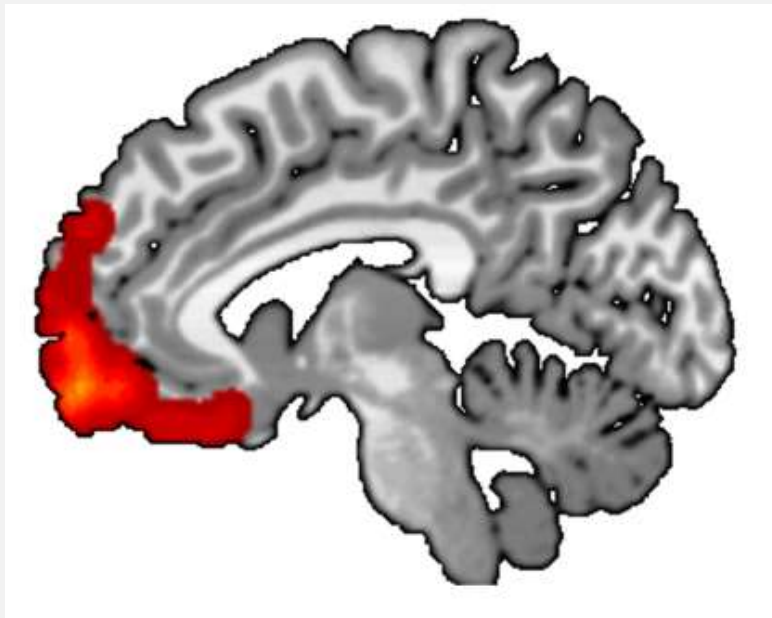
REMEMBER THE ORBITOFRONTAL CORTEX?



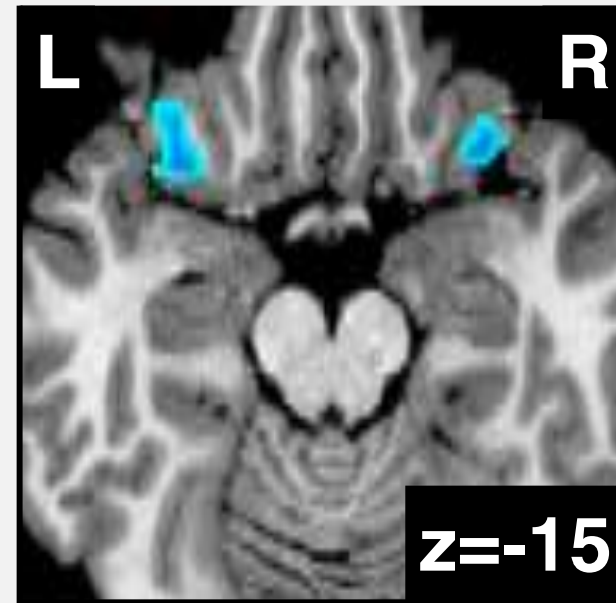
Baxter et al, 1987

Van der Straten et al, 2017

OFC ABNORMALITIES ARE THE MOST CONSISTENT
NEUROIMAGING FINDING IN OCD

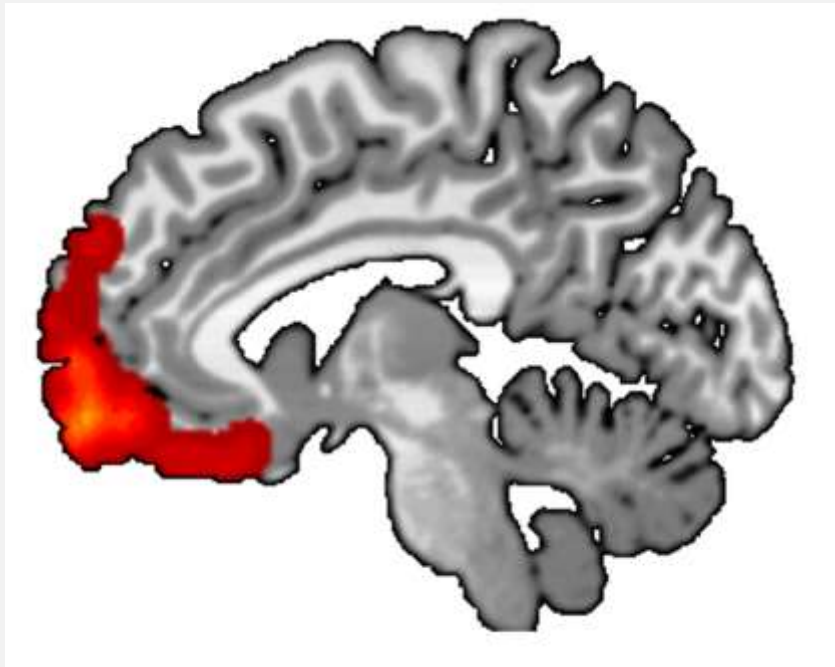


Scheinost et al, 2014

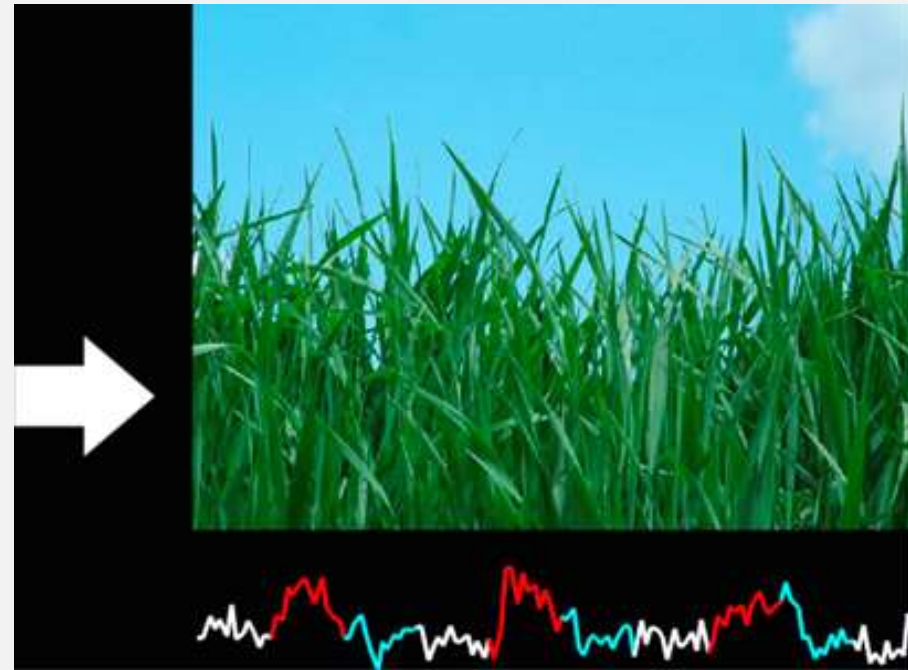


Anticevic et al, 2014

NEUROFEEDBACK – TEACHING PEOPLE TO CONTROL BRAIN ACTIVITY

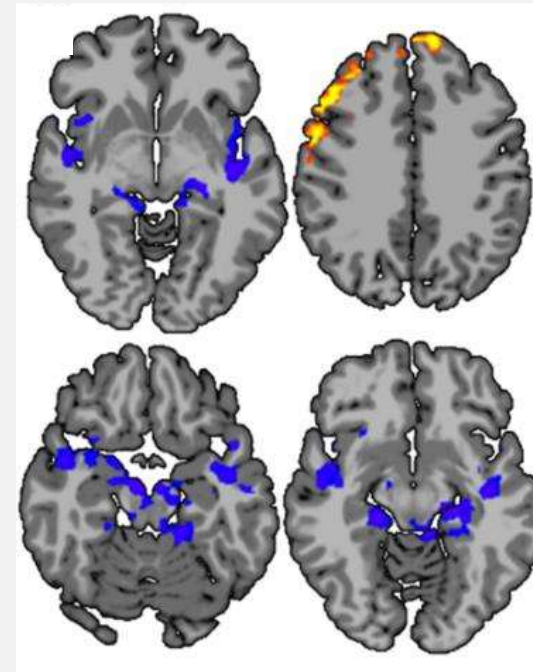
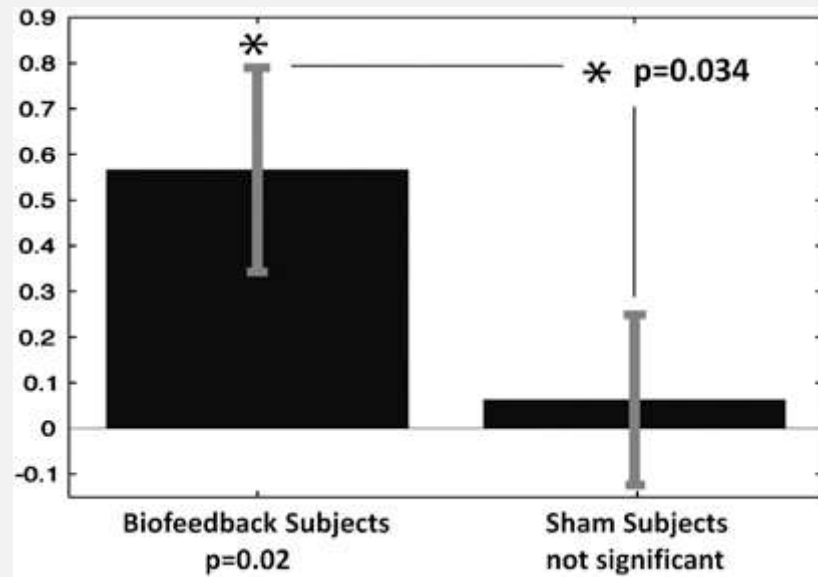


Scheinost et al, 2014



Scheinost et al, 2013

NEUROFEEDBACK – PROOF OF CONCEPT IN SUBCLINICAL CONTAMINATION ANXIETY



Scheinost et al, 2013

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- Vladimir Coric, MD
- Dustin Scheinost, Ph.D.
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