Neurobiology of OCD & Novel Treatment options

Dr. Janardhanan. C. Narayanaswamy M.D.

Consultant- Obsessive Compulsive Disorder Clinic

Wellcome trust-DBT India Alliance Intermediate Fellow
Associate Professor, Department of Psychiatry

National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore

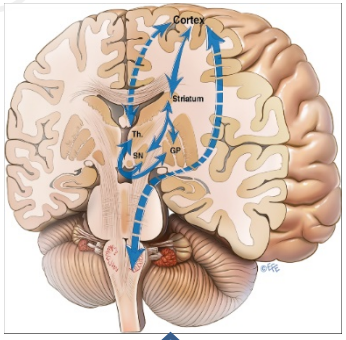
Outline

- Snapshots on Etiology and Pathophysiology
- Cognitive deficits of OCD
- Circuitry Models and Compulsivity
- OCD and the role of anxiety
- Cortical-Subcortical interaction studies
- Neuromodulation: working on the interacting brain networks

NEUROBIOLOGY OF OCD

OCD SYMPTOMS

Neurocognitive aberrations



Neurotransmitters-
Glutamate/Serotonin

Neuroimmune – Cytokines

Vulnerability/genetic

Neurocognitive deficits might form a basis and a template for symptoms

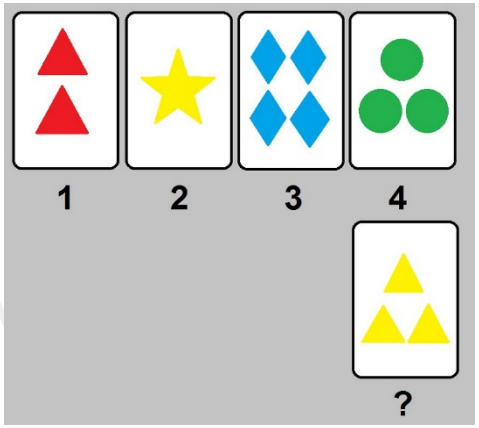
SALIENT NEUROCOGNITIVE DEFICITS IN OCD

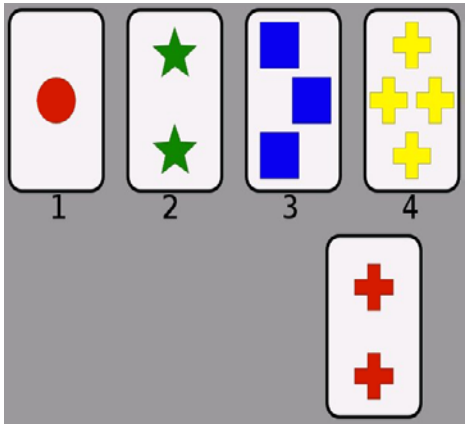
- Stroop task

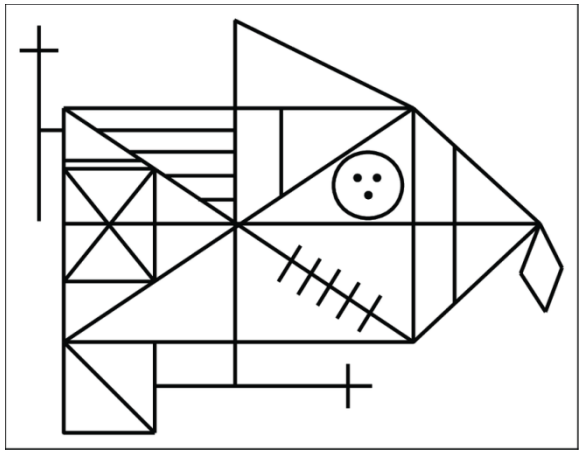
Say the COLOR, not the word:

PURPLE	ORANGE	BLUE
BLUE	RED	PURPLE
BLACK	GREEN	YELLOW
GREEN	BLUE	RED
ORANGE	YELLOW	GREEN

- Wisconsin Card Sorting Test







Complex figure test

SALIENT NEUROCOGNITIVE DEFICITS IN OCD

- Overactive conflict and error detection (cause of obsessions)

  - Stroop task

- Response inhibition/Motor output suppression

  - Go/No-Go, Stop Signal Reaction Time (SSRT) (involves motor suppression in addition to conflict monitoring)

- Set shifting (cognitive inflexibility)

  - attentional switching (WCST, CANTAB ID/ED)

  - affective switching

- Decision making

  - Risk & Uncertainty (IGT)

- Non-verbal memory

  - RCFT

  - Intact copying, poor recall because of executive failure of organizational strategies during encoding

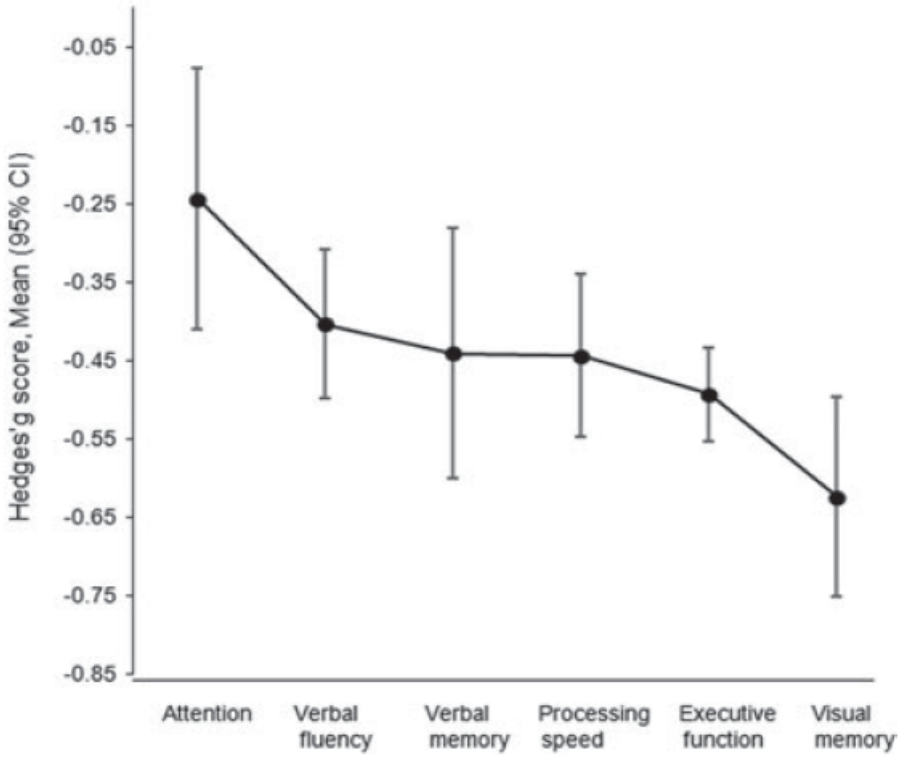
Kuelz , 2004; Nakao 2014

Neuropsychological Deficits in OCD

Meta-analysis – Mean effect sizes (Cohen's d)

- **Non verbal memory** **-0.76**
- **Response inhibition** **-0.49**
- **Set shifting** **-0.51**

Abramovitch et al. 2013



Shin et al. Psychological Medicine 2014

Error Monitoring - Electrophysiology

Contents lists available at ScienceDirect

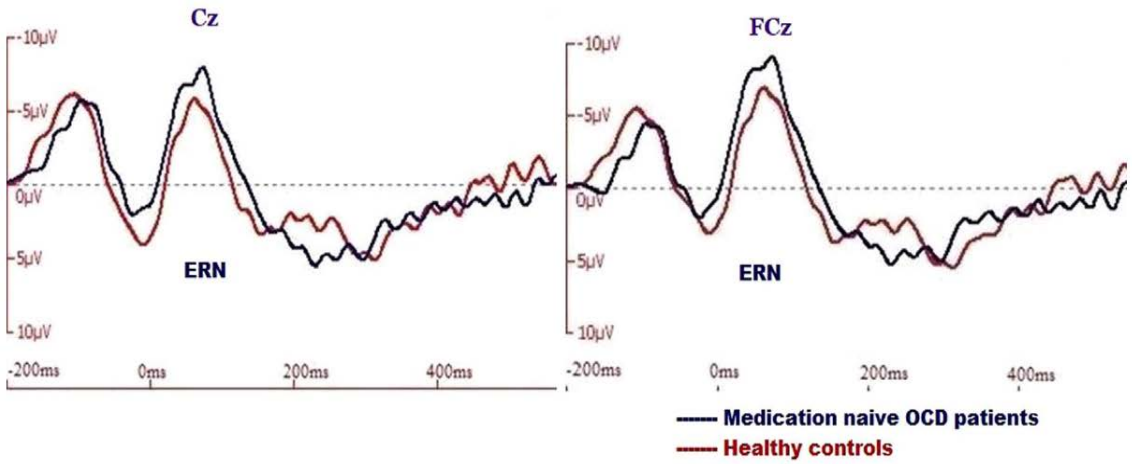
Psychiatry Research

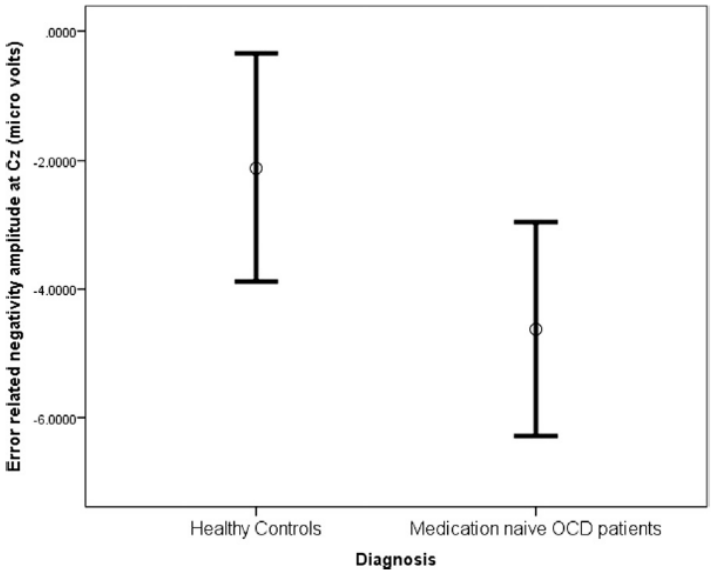
journal homepage: www.elsevier.com/locate/psychres

Enhanced error related negativity amplitude in medication-naïve, comorbidity-free obsessive compulsive disorder

Hema Nawani[b], Janardhanan.C. Narayanaswamy[a,b,*], Shrinivasa Basavaraju[a,b], Anushree Bose[b], Sri Mahavir Agarwal[b], Ganesan Venkatasubramanian[a,b], Y.C. Janardhan Reddy[a]

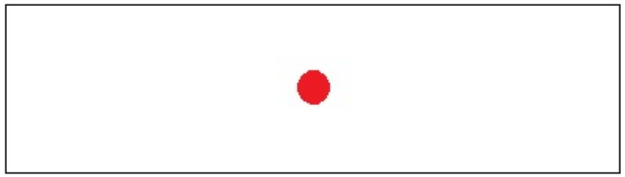
[a] Obsessive Compulsive Disorder Clinic, Department of Psychiatry, National Institute of Mental Health And Neurosciences (NIMHANS), Bangalore, India
[b] Translational Psychiatry Laboratory, Neurobiology Research Center, National Institute of Mental Health And Neurosciences (NIMHANS), Bangalore, India



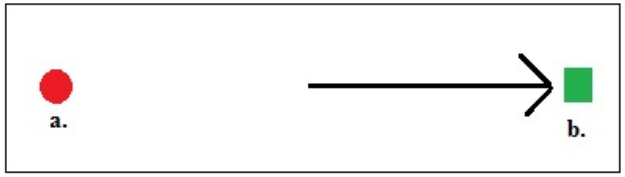


Error monitoring and oculomotor functions

1. Target in the centre of the screen. Eye is looking at target.

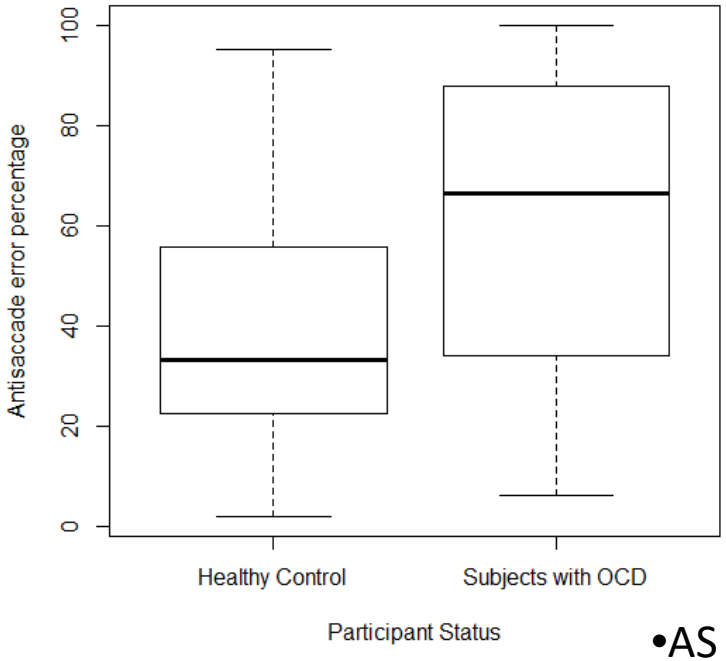


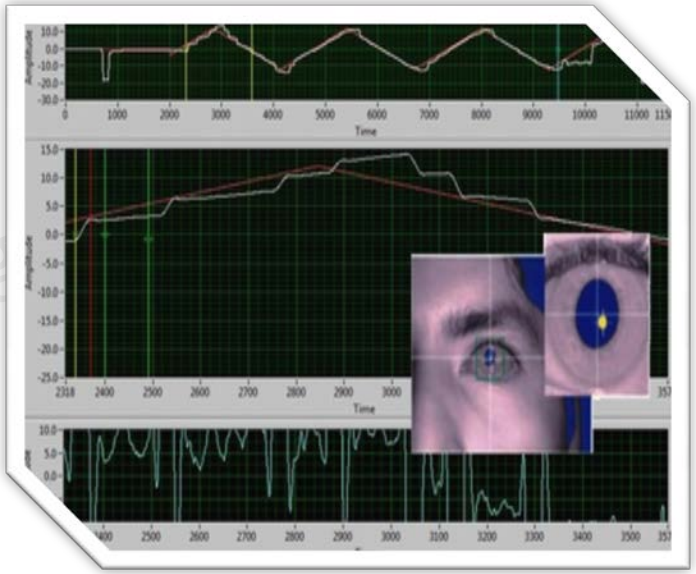
2. Target moves from centre to one side of the screen. Eye should move an equal distance from the centre to the opposite side (mirror image location - direction of arrow).



a - position of the target on the screen
b - correct eye position during an antisaccade

Error monitoring and oculomotor functions





- AS error describes an oculomotor paradigm designed to evaluate the inhibitory capacity of the brain.

- Subjects with OCD made greater number of antisaccade errors which could reflect the fronto-striatal abnormality seen in this condition.

(Narayanaswamy JC, under review)

Neurobiological Models to understand OCD

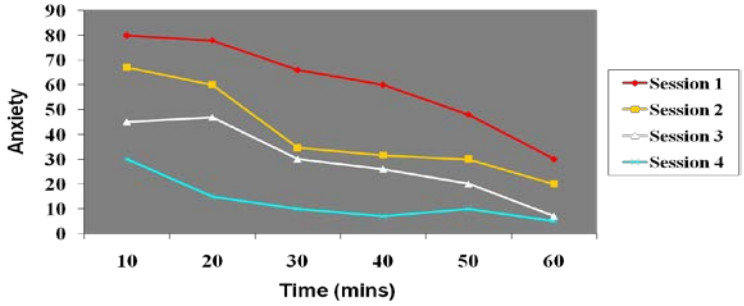
OCD as a compulsive (impulsive) disorder

- repetitive behaviour
- impaired response inhibition
- impaired cognitive ‘top-down’ control
- Decreased function of frontal-striatal circuits

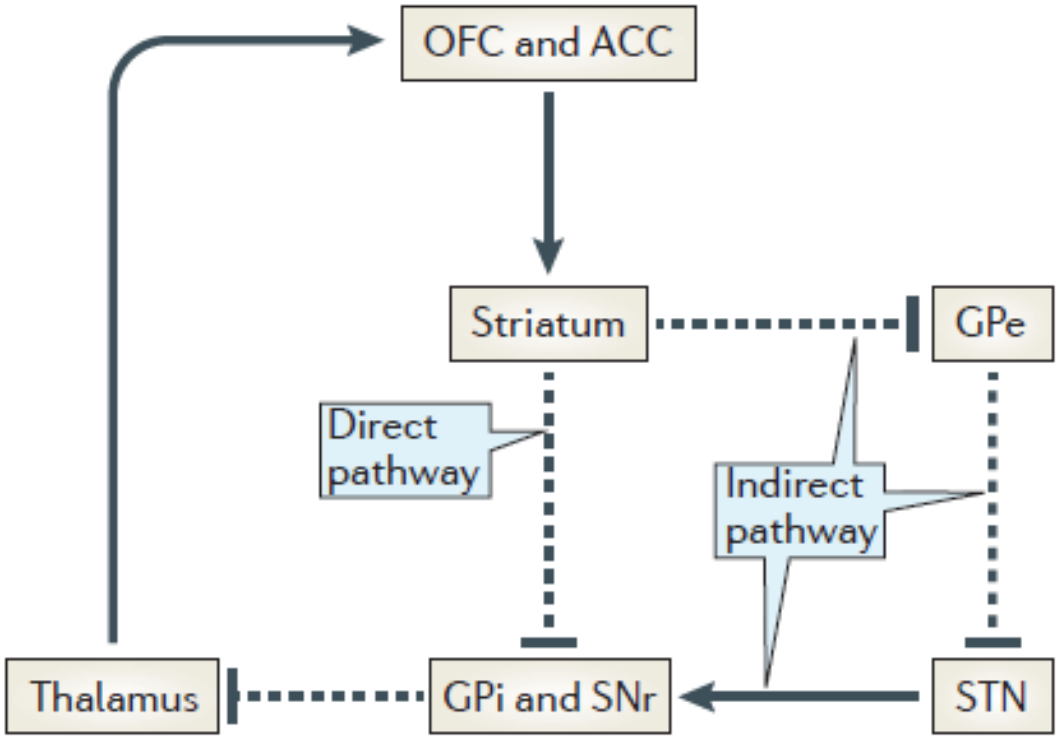
OCD as an anxiety disorder

- harm avoidance / doubt / uncertainty
- anxiety / stress
- Hyper-responsive limbic circuit

Exposure & response prevention



Cortico-Striatal circuitry



Pauls et al, Nature Neuroscience Reviews, 2014

Affective and reward processing

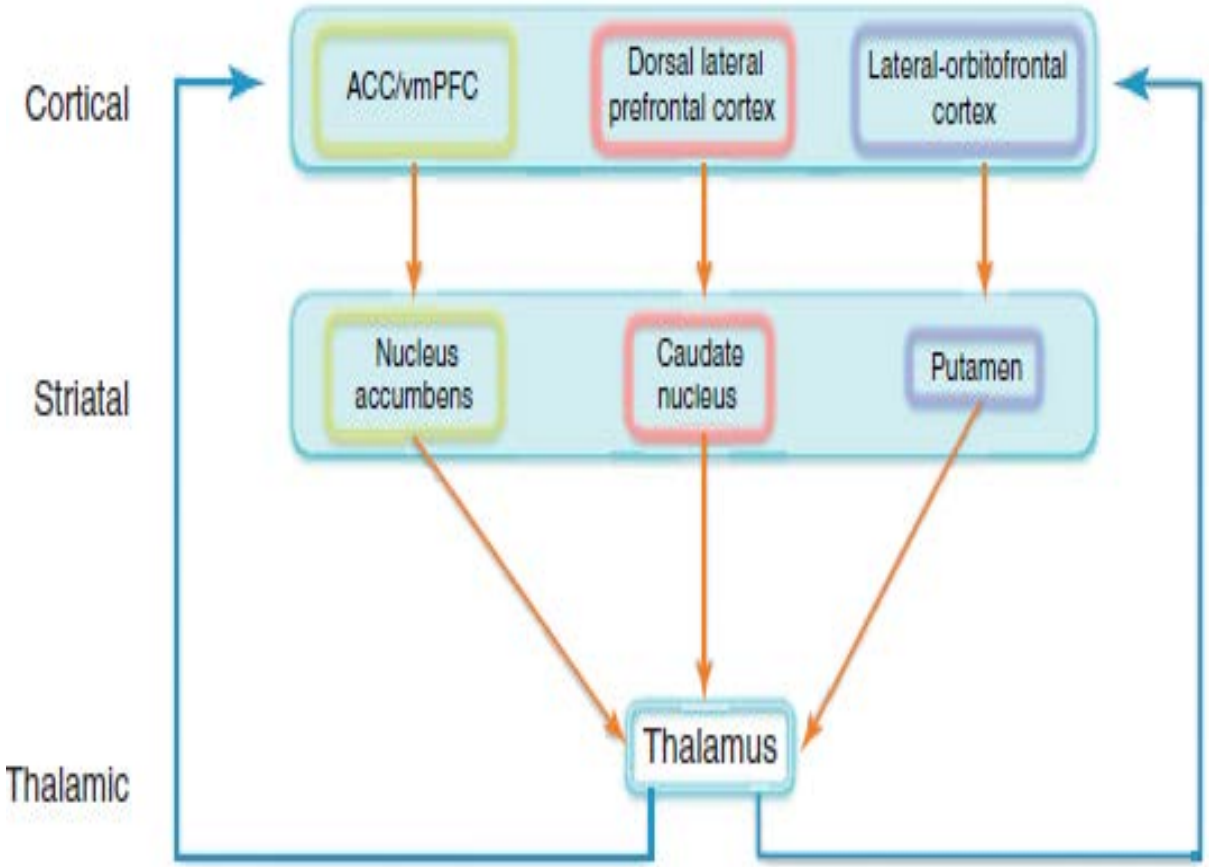
Executive functions- working memory/planning

Motor preparation and response inhibition

Affective

Dorsal cognitive

Ventral cognitive



Milad and Rauch, 2012; Menzies,2008

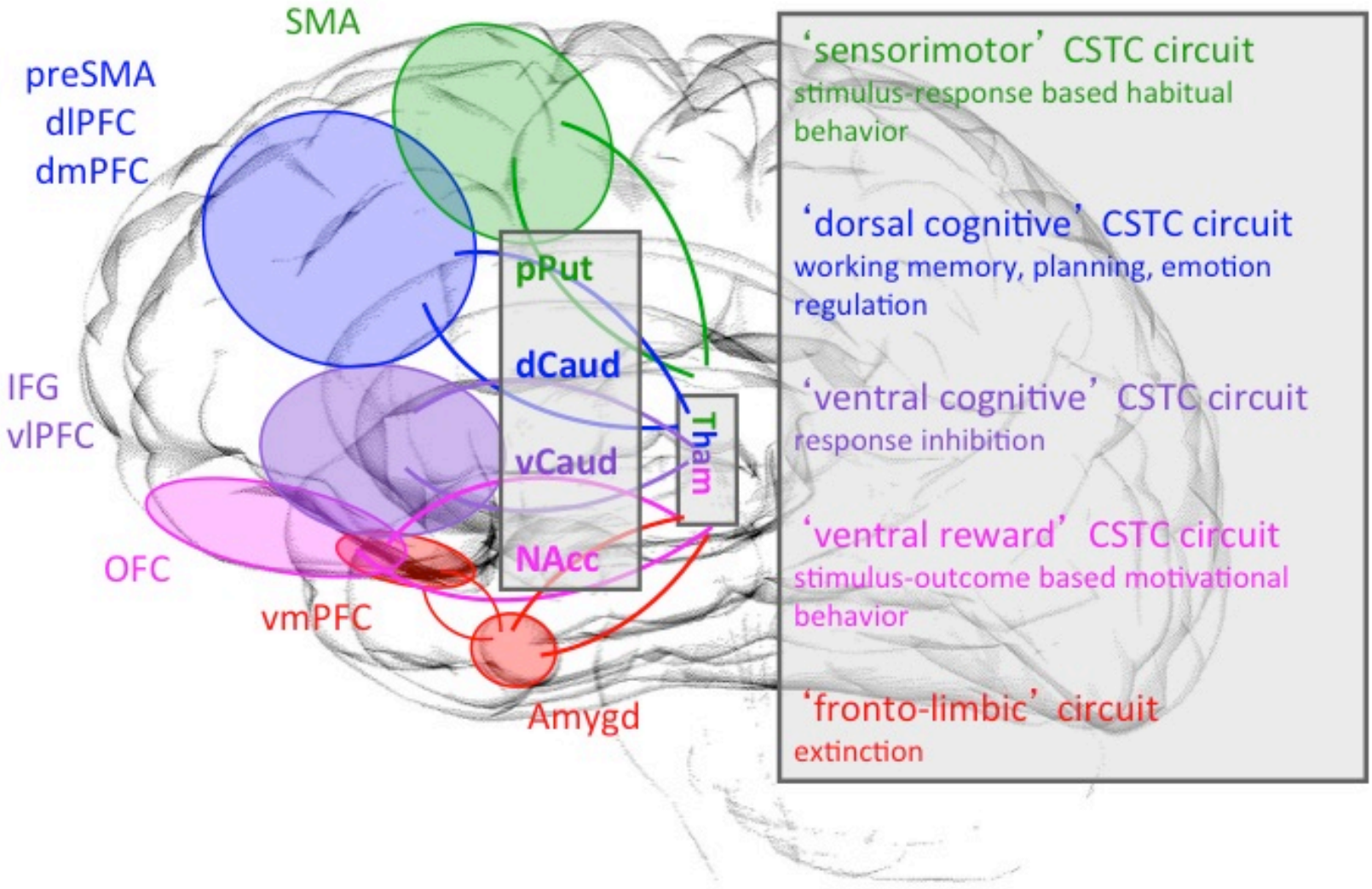
Partially segregated circuits

- **Hyperactive ventral – emotional/motivational circuit** - increased anxiety and repetitive behaviors

- **Hypoactive dorsal executive circuit** -cognitive control deficits and inability to modulate emotional and behavioral responses

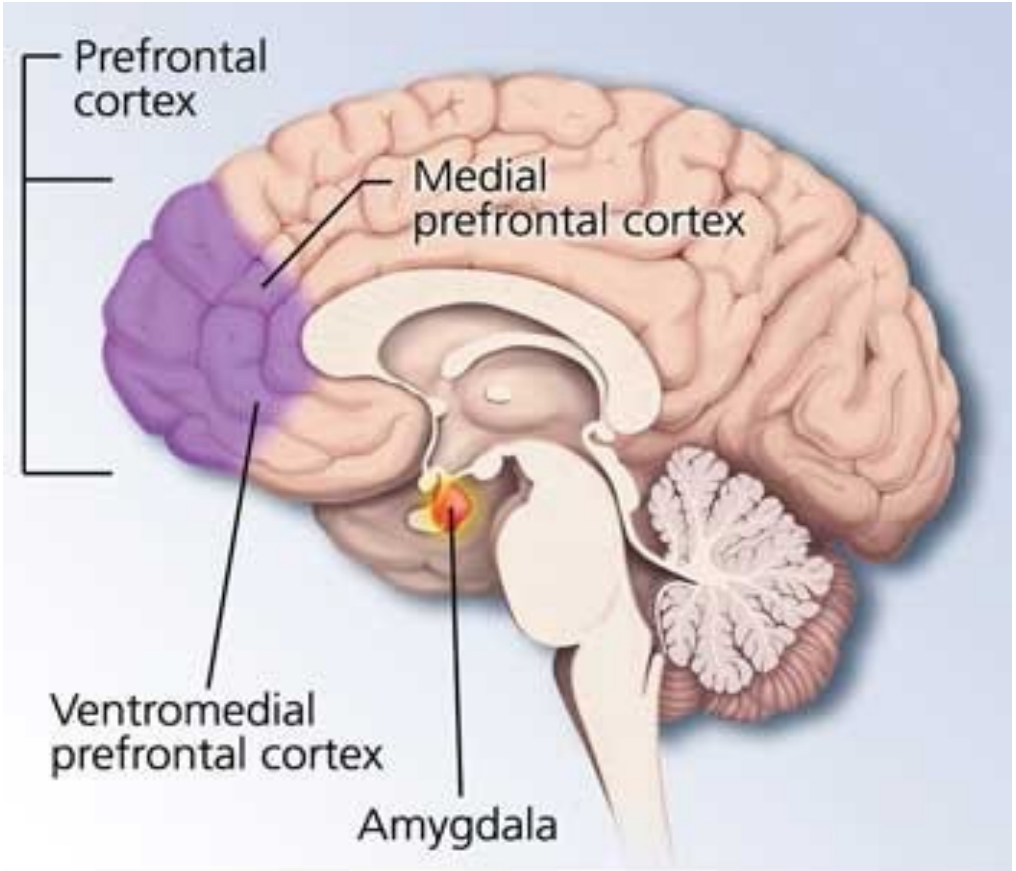
(Phillips etal., 2003; Mataix Cols & van den Heuvel, 2006)

OCD : CSTC CIRCUITS



van den Heuvel et al. 2016, Eur Neuropsychopharmacology

Anxiety in OCD



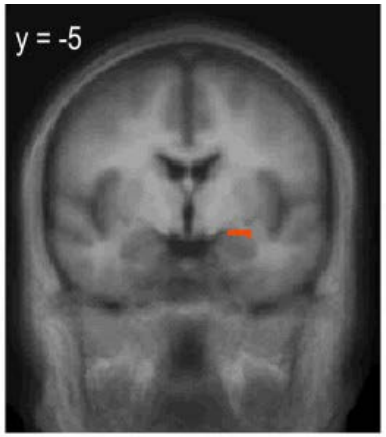
Brain Structures Involved in Dealing with Fear and Stress

DISEASE SPECIFIC STIMULI

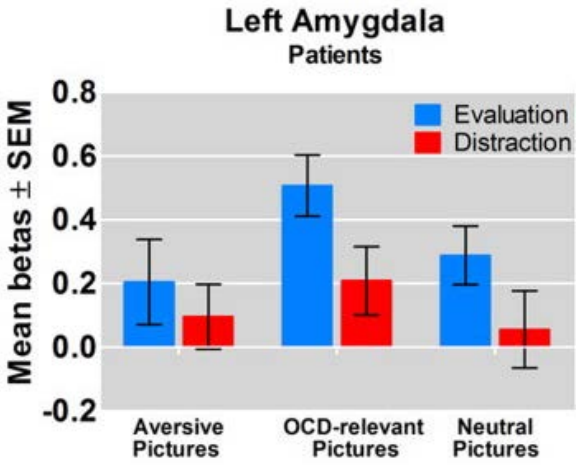
OCD

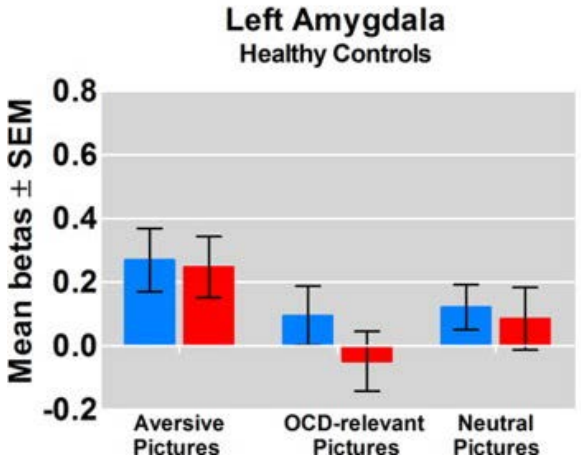
PHOBIA

OCD – SYMPTOM PROVOCATION



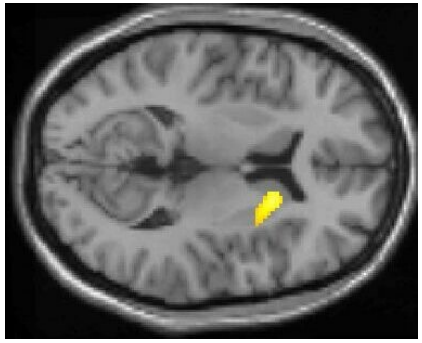
Left Amygdala

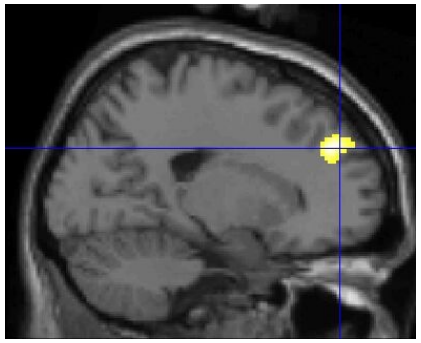




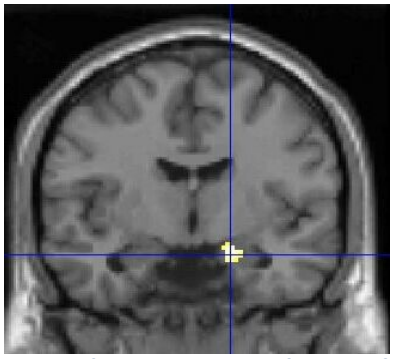
Simon et al, Neuroimage Clin. 2014

controls > OCD: activation dorsal system





OCD > controls :
activation limbic system

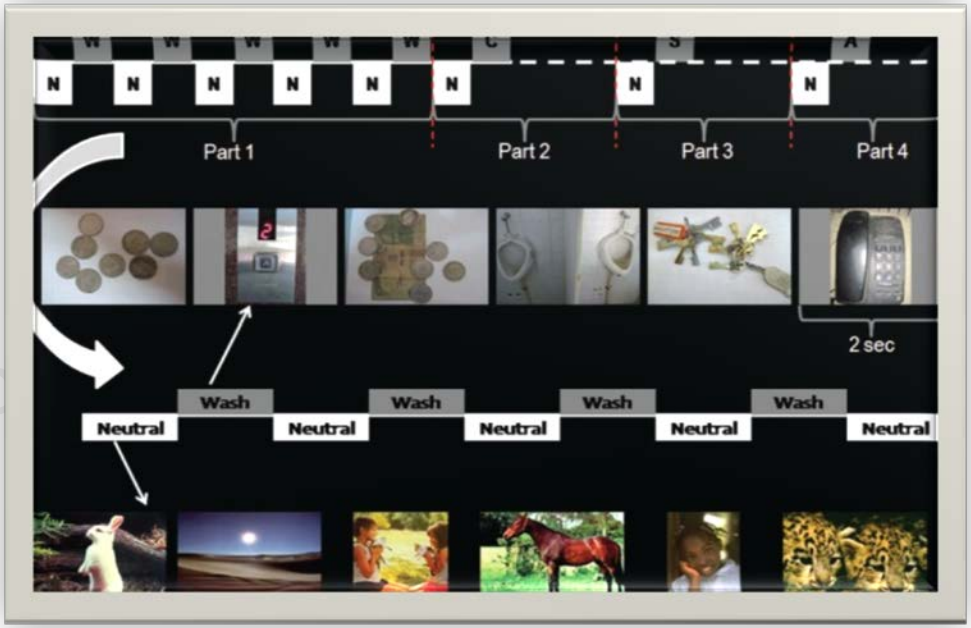


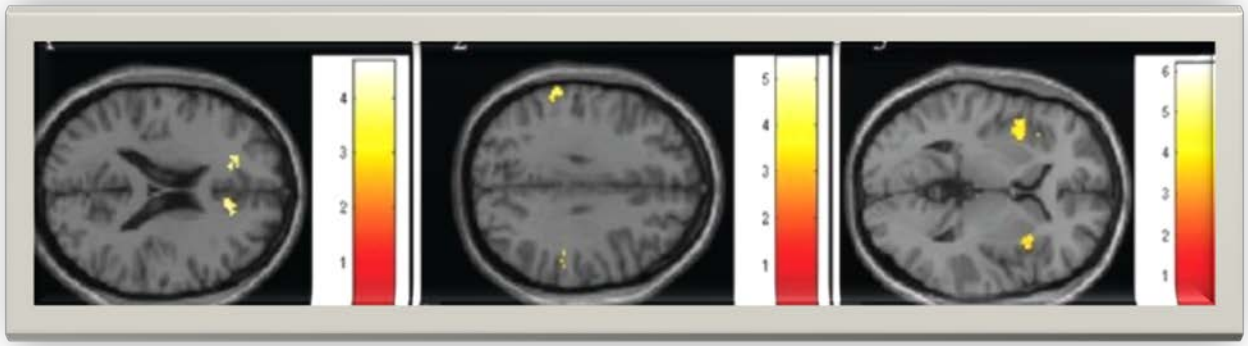
van den Heuvel et al., 2004 Psych Res

OCD- Symptom Provocation fMRI -Washers

Patients were found to have deficient activation in the following areas –

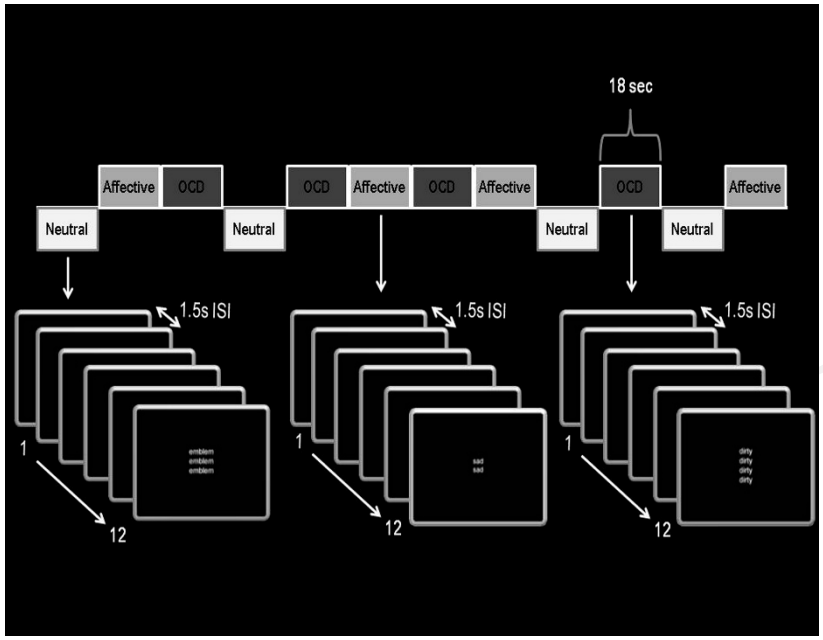
bilateral anterior prefrontal, dorsolateral prefrontal, orbitofrontal, anterior cingulate, insular and parietal cortices, precuneus, and caudate.



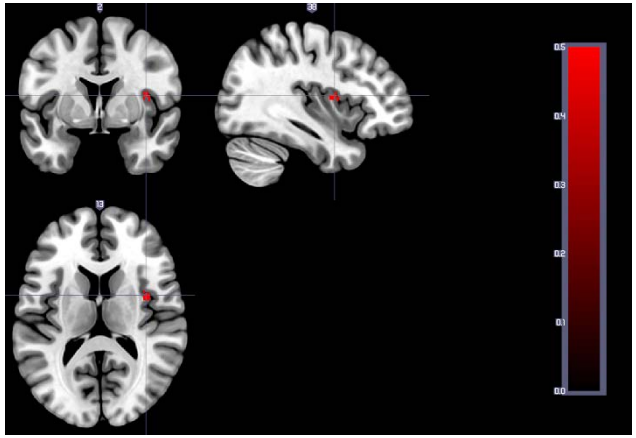


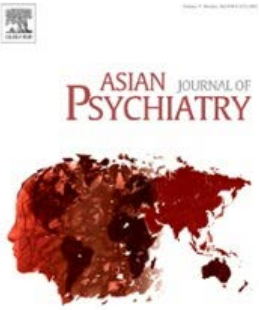
Agarwal SM, 2012

Emotional interference and error monitoring



- Emotional interference is observed in OCD
- This fMRI study examines endophenotype status of emotional interference
- Prefrontal and insular BOLD changes during the task might be an endophenotype





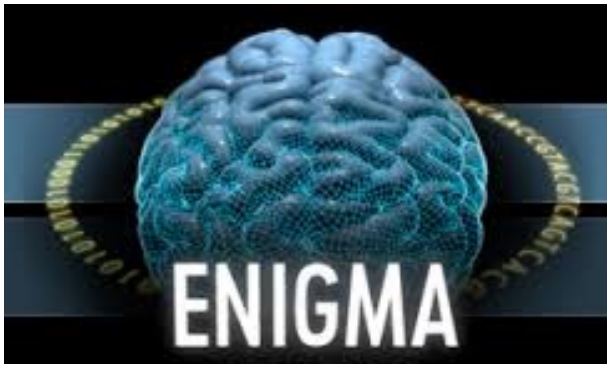
Janardhanan Narayanaswamy et al,
Asian Journal of Psychiatry, 2018

Key Neuroimaging findings on Brain Structure in OCD

ENIGMA-OCD working group

PI's: Odile van den Heuvel / Dan Stein / co-PI: Premika Boedhoe

http://enigma.ini.usc.edu/



Distinct subcortical volume alterations in pediatric and adult OCD:
A worldwide meta- and mega-analysis

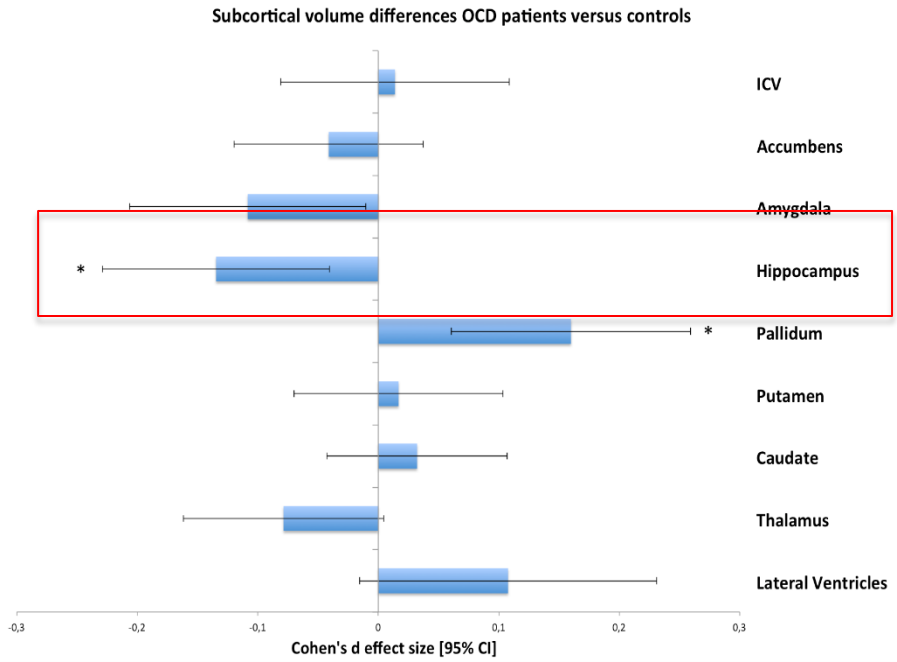
Premika S.W. Boedhoe, M.Sc. (1,2,3), Lianne Schmaal, Ph.D. (1,3), Yoshinari Abe, M.D. (4), Stephanie Ameis, M.D. (5), Paul Arnold, M.D., Ph.D. (6), Marcelo C. Batistuzzo, Ph.D. (7), Francesco Benedetti, M.D. (8), Jan C. Beucke, Ph.D. (9), Irene Bollettini, Psy.D (8), **Anushree Bose**, M.A. (10), Silvia Brem, Ph.D. (11), Anna Calvo, M.Sc. (12), Yuqi Cheng, Ph.D. (13), Kang Ik K. Cho, B.Sc. (14), Sara Dallaspezia, M.D. (8), Damiaan Denys, M.D., Ph.D. (15,16), Kate D. Fitzgerald, M.D. (17), Jean-Paul Fouche, M.Sc. (18,19), Mònica Giménez , Ph.D. (20,21), Patricia Gruner, Ph.D. (22), Gregory L. Hanna, M.D. (17), Derrek P. Hibar, Ph.D. (23), Marcelo Q. Hoexter, M.D., Ph.D. (7), Chaim Huyser, M.D., Ph.D. (24,25), Keisuke Ikari, M.D. (26), Neda Jahanshad, Ph.D. (23), Norbert Kathmann, Ph.D. (9), Christian Kaufmann, Ph.D. (9), Kathrin Koch, Ph.D. (27,28), Jun Soo Kwon, M.D., Ph.D. (14,29), Luisa Lazaro, M.D., Ph.D. (21,30,31,32), Yanni Liu, Ph.D. (17), Christine Lochner, Ph.D. (33), Rachel Marsh, Ph.D. (34,35), Ignacio Martínez-Zalacaín, M.Sc. (20), David Mataix-Cols, Ph.D. (36), José M. Menchón, M.D., Ph.D. (20,21,37), Luciano Minuzzii, M.D., Ph.D. (38), Takashi Nakamae, M.D., Ph.D. (4,39), Tomohiro Nakao, M.D., Ph.D. (26), **Janardhanan C. Narayanaswamy**, M.D. (10), Fabrizio Piras, Ph.D. (40), Federica Piras, Ph.D. (40), Christopher Pittenger, M.D., Ph.D. (22), **Y.C. Janardhan Reddy**, M.D. (10), Joao R. Sato, Ph.D. (41), H. Blair Simpson, M.D., Ph.D. (34,42), Noam Soreni, M.D. (43), Carles Soriano-Mas, Ph.D. (20,21,44), Gianfranco Spalletta, M.D., Ph.D. (40,45), Michael C. Stevens, Ph.D. (46,47), Philip R. Szeszko, Ph.D. (48,49), David F. Tolin, Ph.D. (46,50), **Ganesan Venkatasubramanian**, M.D., Ph.D. (10), Susanne Walitza, M.D., M.Sc. (11), Zhen Wang, M.D., Ph.D. (51,52), Guido A. van Wingen, Ph.D. (15), Jian Xu, Ph.D. (53), Xiufeng Xu, M.D. (13), Je-Yeon Yun, M.D., Ph.D. (29), Qing Zhao, M.D. (51), **ENIGMA-OCD Working-Group***, Paul Thompson, Ph.D. (23), Dan J. Stein, M.D., Ph.D. (33), Odile A. van den Heuvel, M.D., Ph.D. (1,2,3)

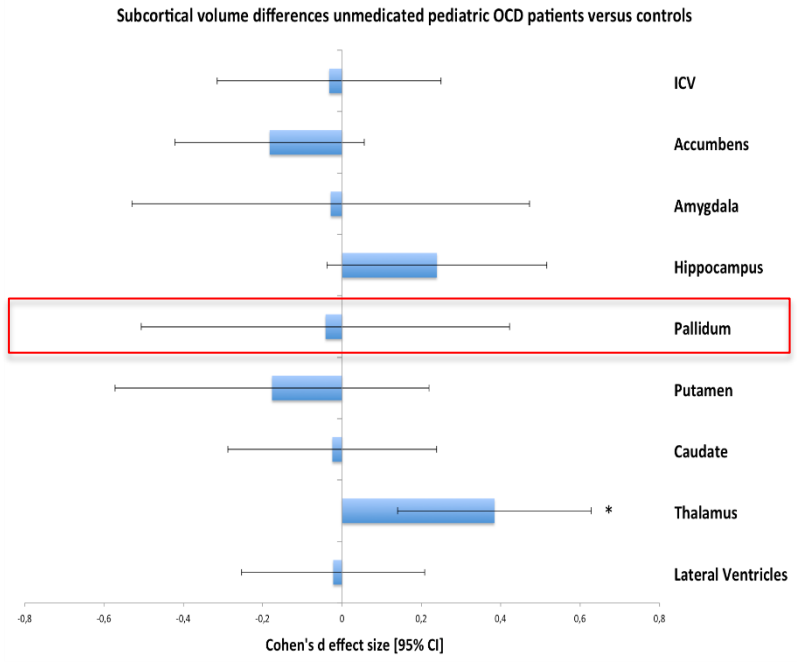
the American Journal of Psychiatry (January 2017)

1,830 OCD patients (N=335 children, N=1,495 adults) and 1,759 controls (N=287 children, N=1,472 adults)

Distinct Subcortical volume alterations in Pediatric and Adult OCD

Boedhoe et al. 2017 (Am J Psych)





Adult OCD vs HC:

- Smaller hippocampus
  (could be related to comorbid depression)
- Larger pallidum
  (related to early disease onset - chronicity)

Juvenile OCD vs HC:

- Larger thalamus
  (unmedicated kids)

CORTICAL ABNORMALITIES

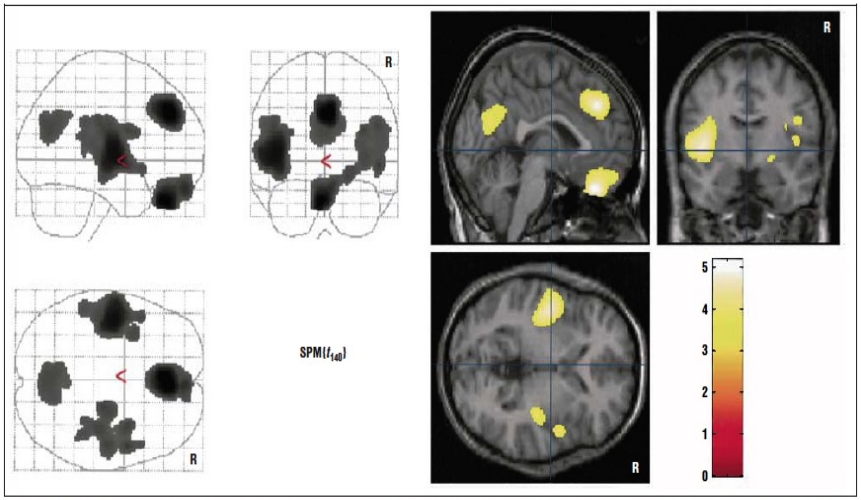


Figure 1. Statistical parametric *t* map (SPM(t_{140})) of gray matter volume reduction in obsessive-compulsive disorder. Clusters of more than 1000 voxels showing uncorrected $P<.001$ are displayed. The 3 orthogonal planes on the left side represent a typical maximum intensity projection "glass brain," and the set of images on the right side illustrate results superimposed on normalized structural images in selected planes. R indicates the right hemisphere, and the color bar represents the *t* score. Significant voxels were found in the orbitofrontal cortex, medial frontal gyrus, and left insulo-opercular region (corrected $P<.05$). Note that right insular and retrosplenial changes, showing a tendency toward significance, are also displayed.

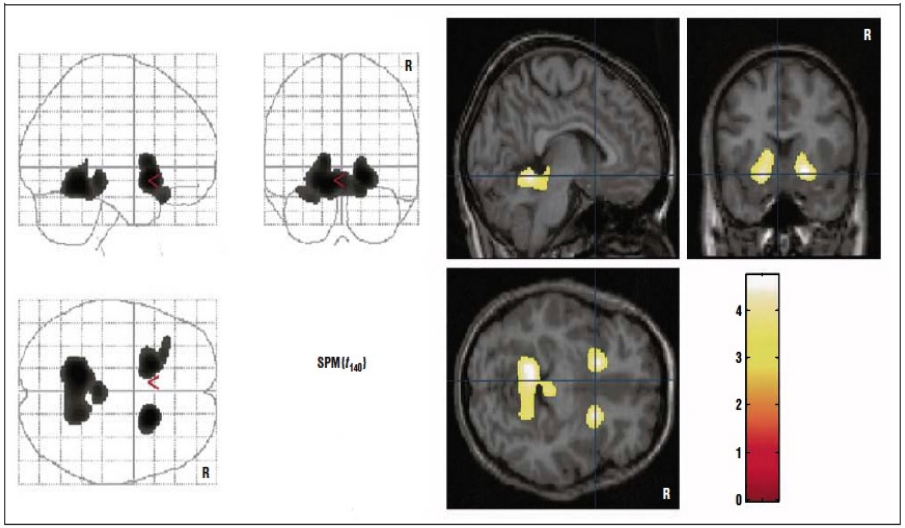


Figure 2. Statistical parametric *t* map (SPM(t_{140})) showing relative increases in gray matter volume in obsessive-compulsive disorder. Clusters of more than 1000 voxels at $P<.001$ are displayed. R indicates the right hemisphere, and the color bar represents the *t* score. Significant voxels were found in the ventral part of the striatum, including the ventral striatum proper area, and in the anterior cerebellum (corrected $P<.05$).

Decreased gray matter volume

Increased gray matter volume

72 OCD Vs. 72 HC

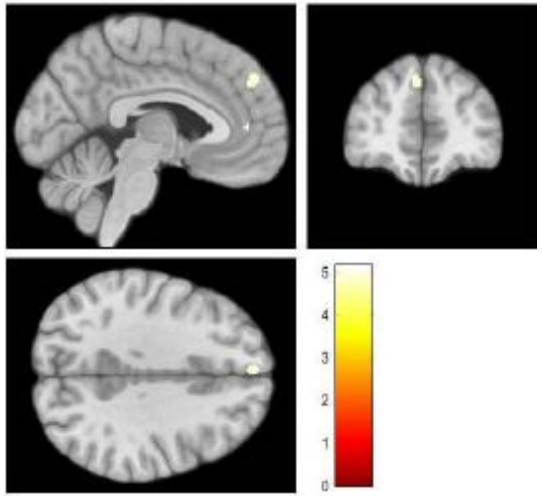
Pujol et al. 2004; Arch Gen Psych

CORTICAL ABNORMALITIES

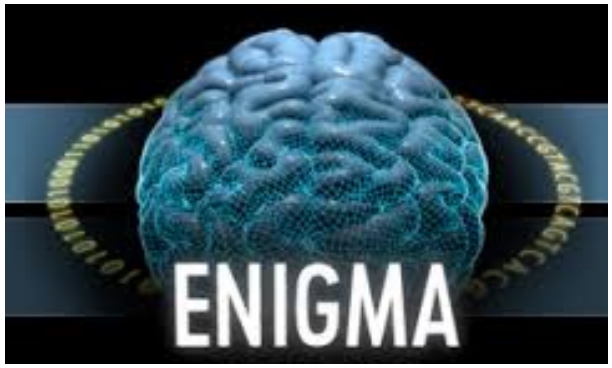
Data from OCD Clinic, NIMHANS (Unpublished):
221 DSM-IV OCD patients with the Y-BOCS ≥ 16 [Unmedicated = 142 (drug-naive =94, drug-free for at least 2 months = 48)] and 194 HC

1.

Contrast	MNI Coordinate	Cluster Extent (K_E)	T	P_{FWE}	Region
Healthy Controls > Medicated OCD Patients	-8 44 6	50	5.03	0.006	Left ACC (Brodmann area 32)
	-5 48 36	91	5	0.011	Left Medial Frontal Gyrus (Brodmann area 8)



2. **Unmedicated OCD vs. HC = No differences**



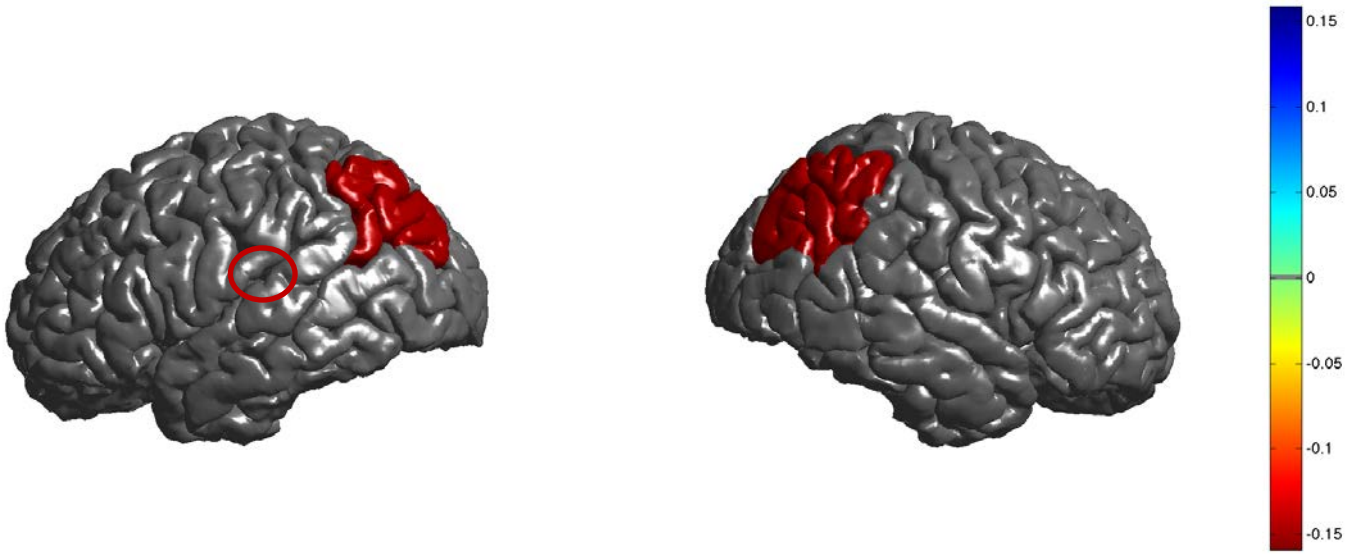
Cortical Abnormalities Associated With Pediatric and Adult Obsessive-Compulsive Disorder: Findings From the ENIGMA Obsessive-Compulsive Disorder Working Group.

Boedhoe PSW[1], Schmaal L[1], Abe Y[1], Alonso P[1], Ameis SH[1], Anticevic A[1], Arnold PD[1], Batistuzzo MC[1], Benedetti F[1], Beucke JC[1], Bollettini I[1], **Bose A**[1], Brem S[1], Calvo A[1], Calvo R[1], Cheng Y[1], Cho KIK[1], Ciullo V[1], Dallaspezia S[1], Denys D[1], Feusner JD[1], Fitzgerald KD[1], Fouche JP[1], Fridgeirsson EA[1], Gruner P[1], Hanna GL[1], Hibar DP[1], Hoexter MQ[1], Hu H[1], Huyser C[1], Jahanshad N[1], James A[1], Kathmann N[1], Kaufmann C[1], Koch K[1], Kwon JS[1], Lazaro L[1], Lochner C[1], Marsh R[1], Martínez-Zalacaín I[1], Mataix-Cols D[1], Menchón JM[1], Minuzzi L[1], Morer A[1], Nakamae T[1], Nakao T[1], **Narayanaswamy JC**[1], Nishida S[1], Nurmi E[1], O'Neill J[1], Piacentini J[1], Piras F[1], Piras F[1], **Reddy YCJ**[1], Reess TJ[1], Sakai Y[1], Sato JR[1], Simpson HB[1], Soreni N[1], Soriano-Mas C[1], Spalletta G[1], Stevens MC[1], Szeszko PR[1], Tolin DF[1], van Wingen GA[1], **Venkatasubramanian G**[1], Walitza S[1], Wang Z[1], Yun JY[1]; **ENIGMA**-OCD Working Group[1], Thompson PM[1], Stein DJ[1], van den Heuvel OA[1]; **ENIGMA** OCD Working Group.

American Journal of Psychiatry, 2018

ENIGMA-OCD Cortical Analysis

adult OCD (N=1498) vs HC (N=1436)



↓ cortical thickness of bilateral inferior parietal cortex

↓ surface area of left transverse temporal cortex

Bodhoe et al., 2018

SUMMARY

Boedhoe et al., 2018

Cortical:

- smaller volume in dorsomedial PFC, bilateral insula, and parietal cortex
- bigger volume in cerebellum
- cortical effects seem to be dependent on medication status

Subcortical:

- bigger pallidum in adults, mostly in case of disease chronicity
- smaller hippocampus in adults, mostly related to comorbid depression
- bigger thalamus in (unmedicated) children, not in adults

Changes due to chronic compulsivity? Due to medication?

CORTICAL – SUBCORTICAL REGULATORY EFFECTS?

Cognitive Appraisal during Symptom Provocation

Psychological Medicine

cambridge.org/psm

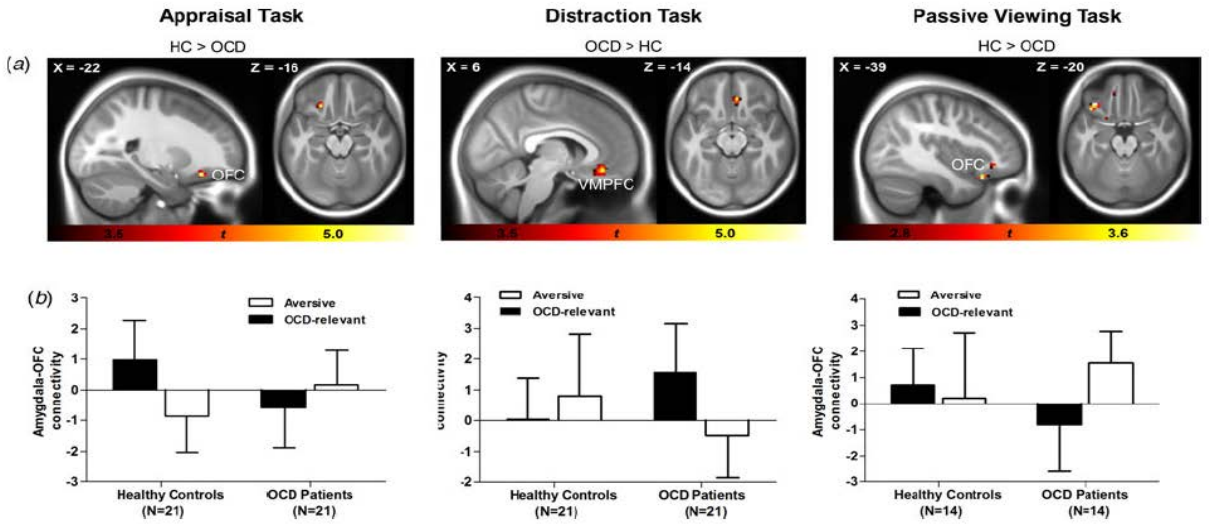
2017

Original Article

Amygdala–prefrontal connectivity during appraisal of symptom-related stimuli in obsessive–compulsive disorder

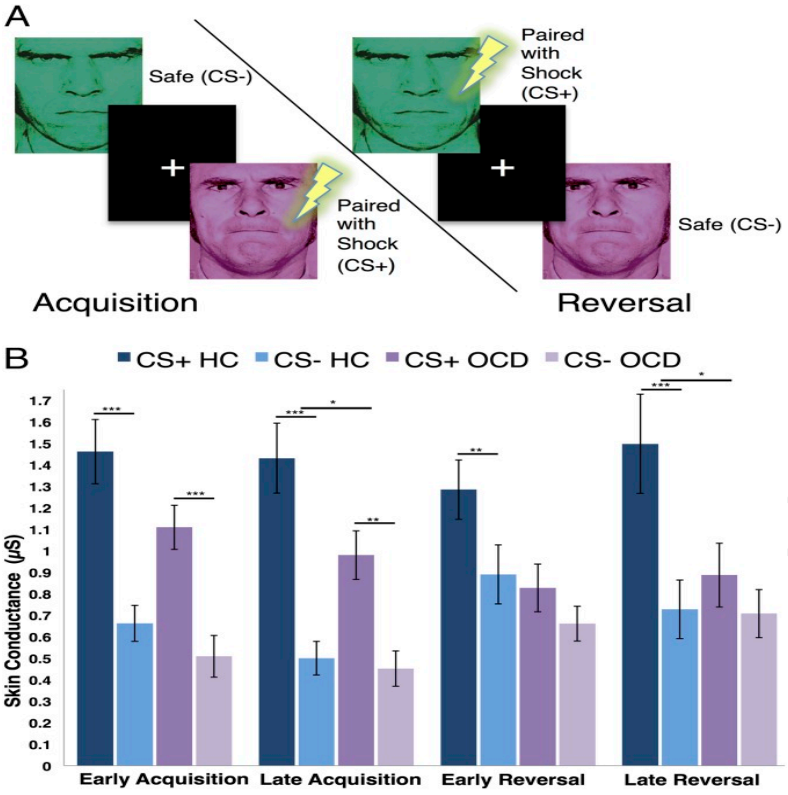
Sandra Paul[1], Jan C. Beucke[1,2], Christian Kaufmann[1], Anna Mersov[3], Stephan Heinzel[1,*], Norbert Kathmann[1] and Daniela Simon[1]

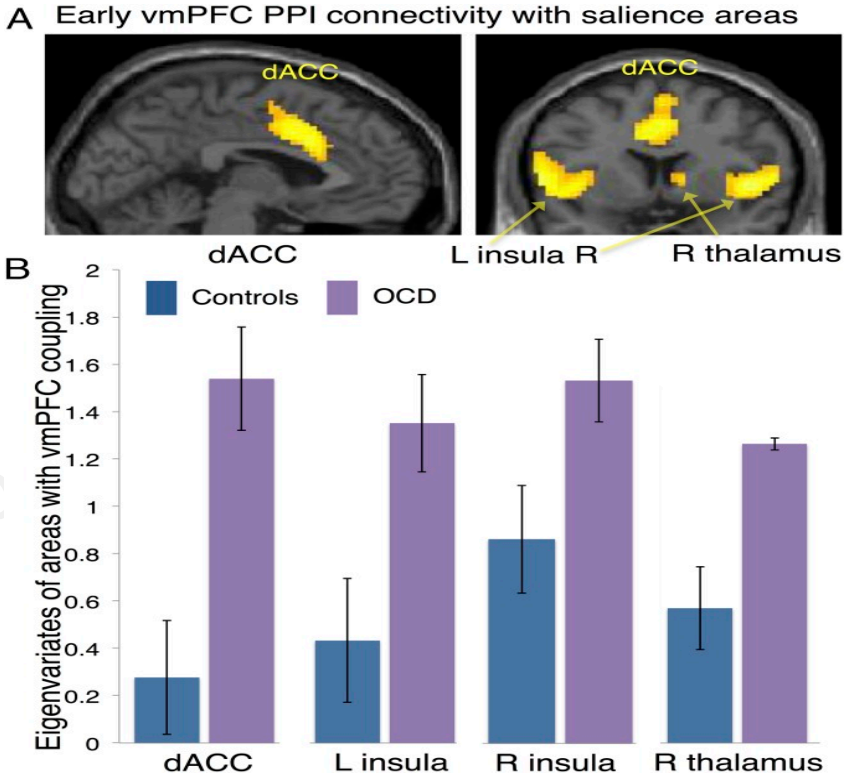
*Stephan Heinzel is now at the Department of



- During symptom provocation ---- Reductions in positive coupling between amygdala and orbitofrontal cortex were observed in OCD patients relative to healthy control participants
- During appraisal and passive viewing of OCD-relevant stimuli - abnormally high Amygdala-ventromedial prefrontal cortex coupling was found when appraisal was distracted by a secondary task.
- No group differences in amygdala connectivity at rest.

Fear Extinction Paradigm





Fear reversal paradigm:

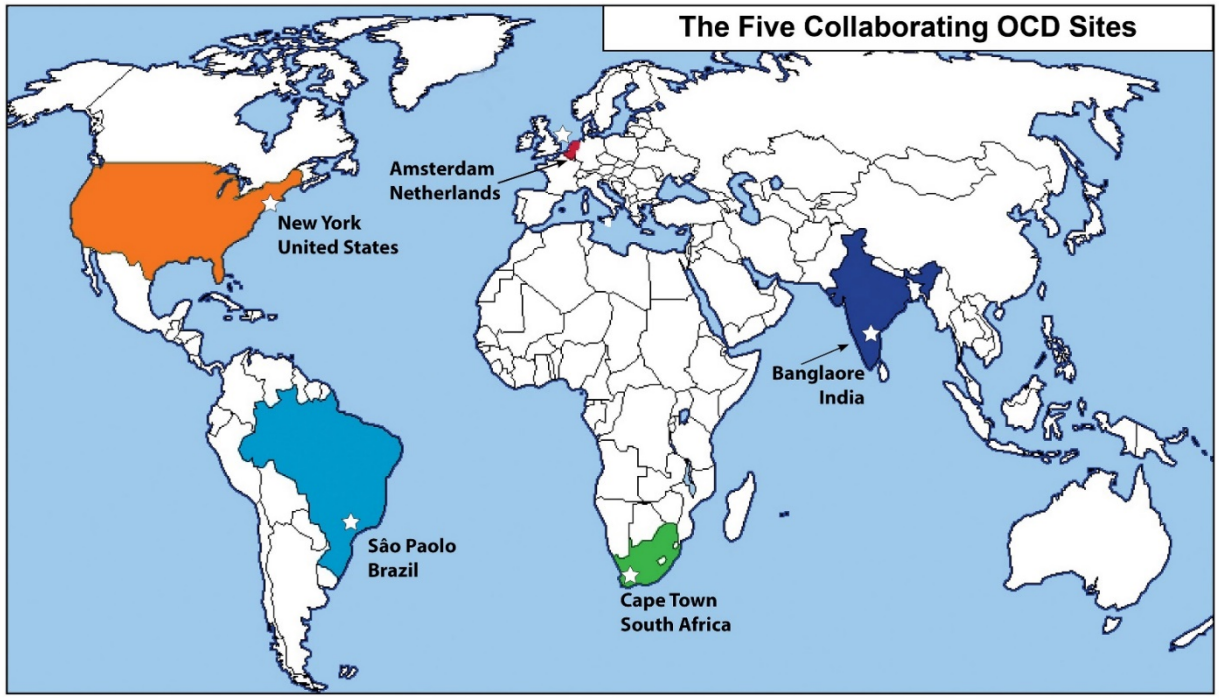
Maladaptive vmPFC combined with increased connectivity with areas involved in salience processing undermines accurate safety learning in OCD patients, resulting in inflexible threat beliefs.

Apergis-Schoute et al., **Neural basis of impaired safety signaling in Obsessive Compulsive Disorder** Proc Natl Acad Sci U S A. 2017

Identifying reproducible bio-signatures of OCD

Aim #1: To identify neuroimaging signatures using data-driven approaches.

Aim #2: To link these signatures to neurocognitive function and clinical dimensions.



R01 MH113250 – PI- Prof. Blair Simpson (USA)

Role of neuroplasticity in treatment – Modulating effect of glutamate

Evidence for glutamatergic abnormalities in OCD

- Elevated CSF glutamate
- In vivo studies – MRS
- Genetic studies

Evidence for glutamatergic abnormalities in OCD

Elevated CSF glutamate

Neuropsychopharmacology (2009) 34, 2489–2496

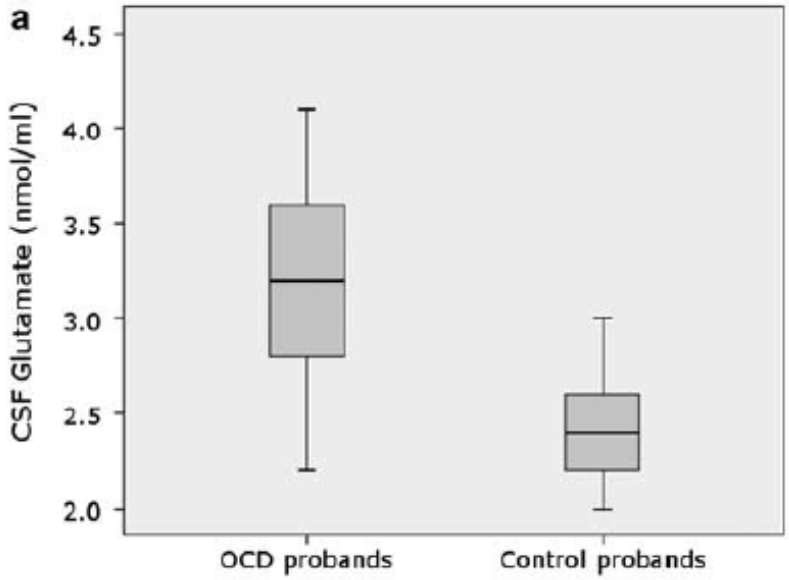
www.neuropsychopharmacology.org

Anti-Brain Autoantibodies and Altered Excitatory Neurotransmitters in Obsessive–Compulsive Disorder

Sagnik Bhattacharyya[1,*], Sumant Khanna[2], Koushik Chakrabarty[3], Anita Mahadevan[4], Rita Christopher[5] and SK Shankar[4]

- In a subset of OCD patients – excessive glutamate in CSF

  (Chakrabarty et al, 2005; Bhattacharya et al., 2009)
- Only a subset of cases of OCD ?
- Global / region specific alterations ?



Evidence for glutamatergic abnormalities in OCD

Magnetic Resonance Spectroscopy Studies

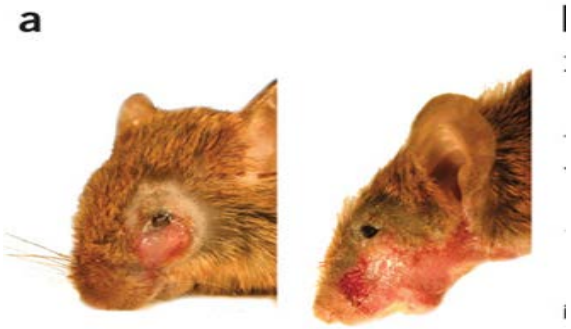
- Early MRS studies in unmedicated pediatric OCD - glutamate and related compounds elevated in the basal ganglia ; reduced in the ACC (Rosenberg et al., 2000 & 2004)
- Recent studies have reported variable results, with the majority reporting no significant differences between patients and controls (review - Brennan et al., 2013)

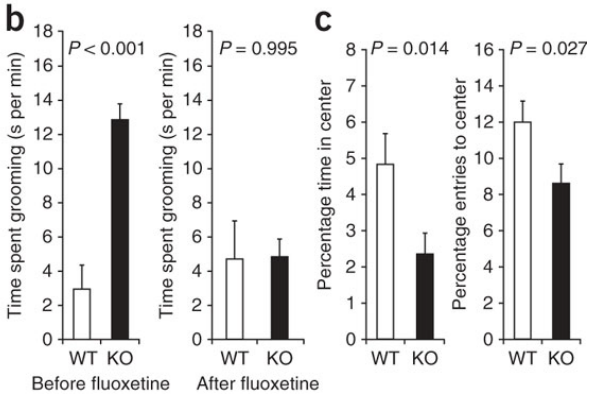
Evidence for glutamatergic abnormalities in OCD
Genetics

- Attempts to demonstrate etiological role for glutamate dysregulation in OCD
- Slc1a1, which encodes the principle neuronal glutamate transporter, EAAT3
- **Recent focus of interest :**
- Genes that are highly expressed in cortico-striatal circuits
- Sapap3 knockout mouse (Welch 2007) ;

Slitrk5 knockout mouse (Shmelkov, Nat Med 2014)

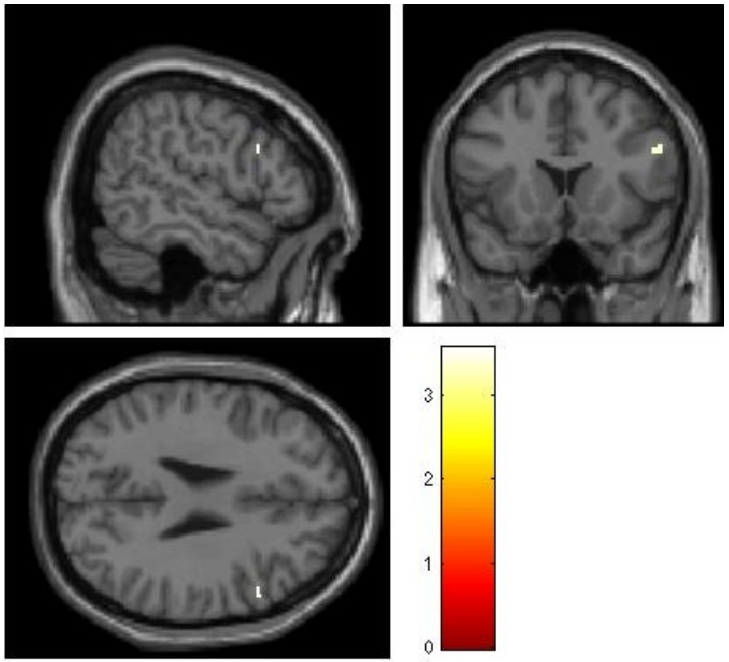
- Key components of the postsynaptic complex that anchors and spatially organizes glutamate receptors





Glutamatergic – genetics & imaging

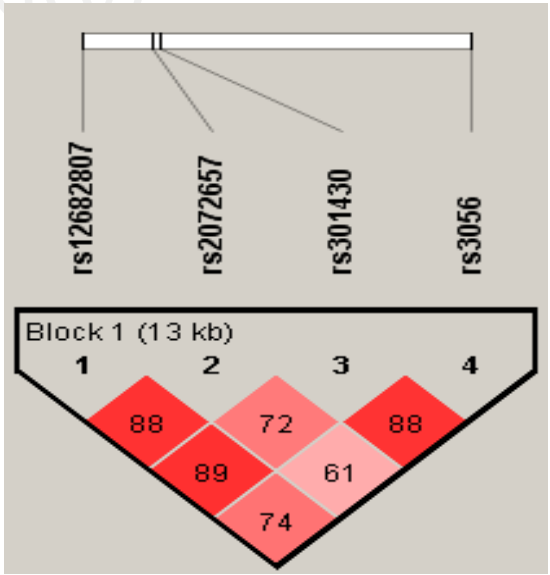
Comparison between regional gray matter volume in OCD patients and Healthy controls : Modulated By SLC1A1 rs3056 (A/G) Genotype (N=160) and healthy controls (N=152)



MNI co-ordinates: (X= 54 Y= 17 Z=27); T=3.57;BA =9; $p_{svc\text{-}fwe,<0.05}$)

Significantly less gray matter volume in Right Middle Frontal Gyrus in G allele carriers in patients

SLC1A1 [rs12682807,2072657,301430,3056] Single marker and Haplotype association with Patients and Controls



Jose et al., unpublished

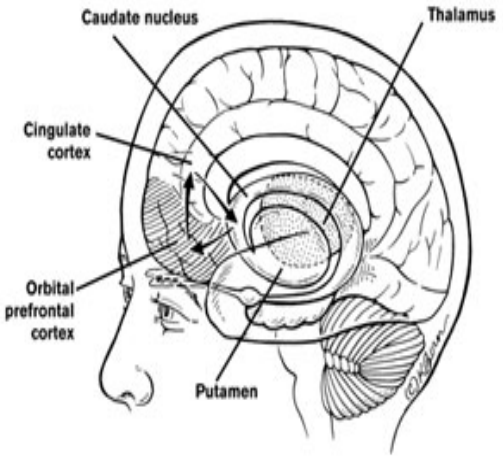
TRANSLATING EVIDENCE FROM NEURAL CIRCUITRY MODELS OF OCD

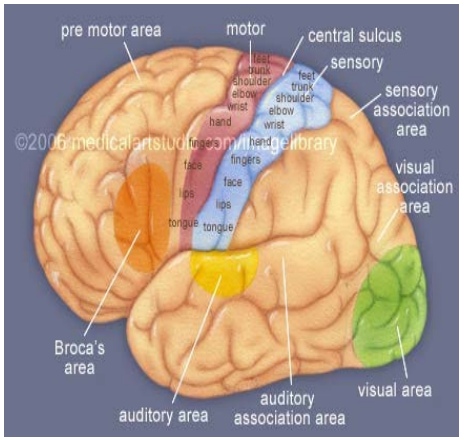
Neuromodulatory approaches

- Repetitive transcranial magnetic stimulation (rTMS)
- Transcranial direct current stimulation (tDCS)

rTMS

- **Advantages -** More focal stimulation, non-invasive, no need for anesthesia
- **Disadvantages** - most available systems target superficial targets





High frequency –excitatory & Low frequency - inhibitory

Obsessive Compulsive Disorder- rTMS targets

Targets	Remarks
Dorsolateral prefrontal cortex (DLPFC)	• Rationale: positive studies in depression and imaging studies • Inconsistent responses for both HF and LF rTMS on either side
Pre-Supplementary motor Area (Pre-SMA)	• Hyperactivity noticed in functional imaging studies • Early positive studies with LF rTMS • Later studies with larger sample size were not encouraging • Interest in high frequency – ? hyperactivity is compensatory
Orbitofrontal cortex (OFC)	• Hyperactivity of orbitofrontal cortex- more consistently seen in OCD • Pilot studies have shown positive findings • Targets ill-defined
Dorsomedial prefrontal cortex (DMPFC)	• Recent evidence from imaging studies • Open-label trials with both HF and LF • Needs special coils

Current evidence for rTMS in OCD

- Most meta-analyses have demonstrated significant short term efficacy in comparison to placebo
  - 18 RCTs with Hedge's g of 0.79 (0.43 – 1.15)
  - Pre-SMA generally showing the best response
    Rehn et al, 2018

- However inconsistent results from recent studies
- Long term efficacy not established
- Should be considered an experimental treatment and can be tried in SSRI non-responsive patients

Transcranial direct current stimulation (tDCS)

- Battery and 2 electrodes
  - weak current passed between anode and cathode
- **Anode** - increases excitability and spontaneous neural activity
- **Cathode** - decreases excitability and spontaneous neural activity

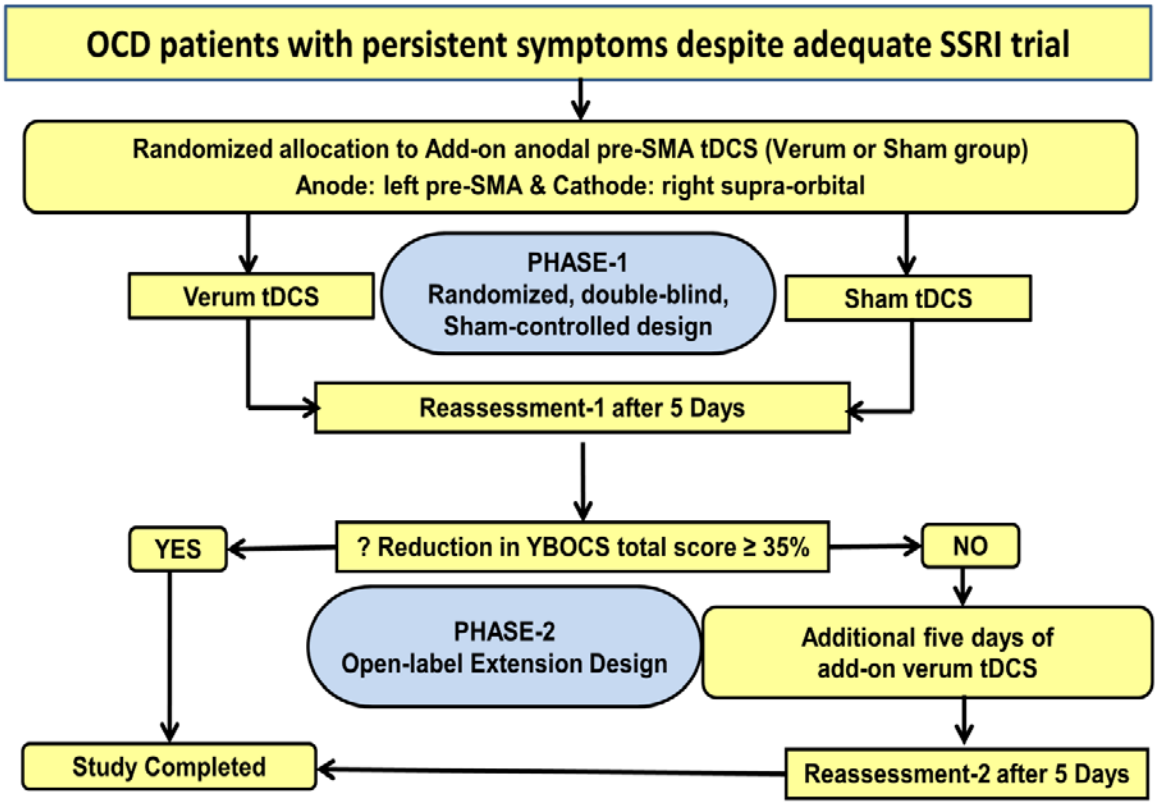
- Cheap, portable, non-invasive and minimal adverse effects

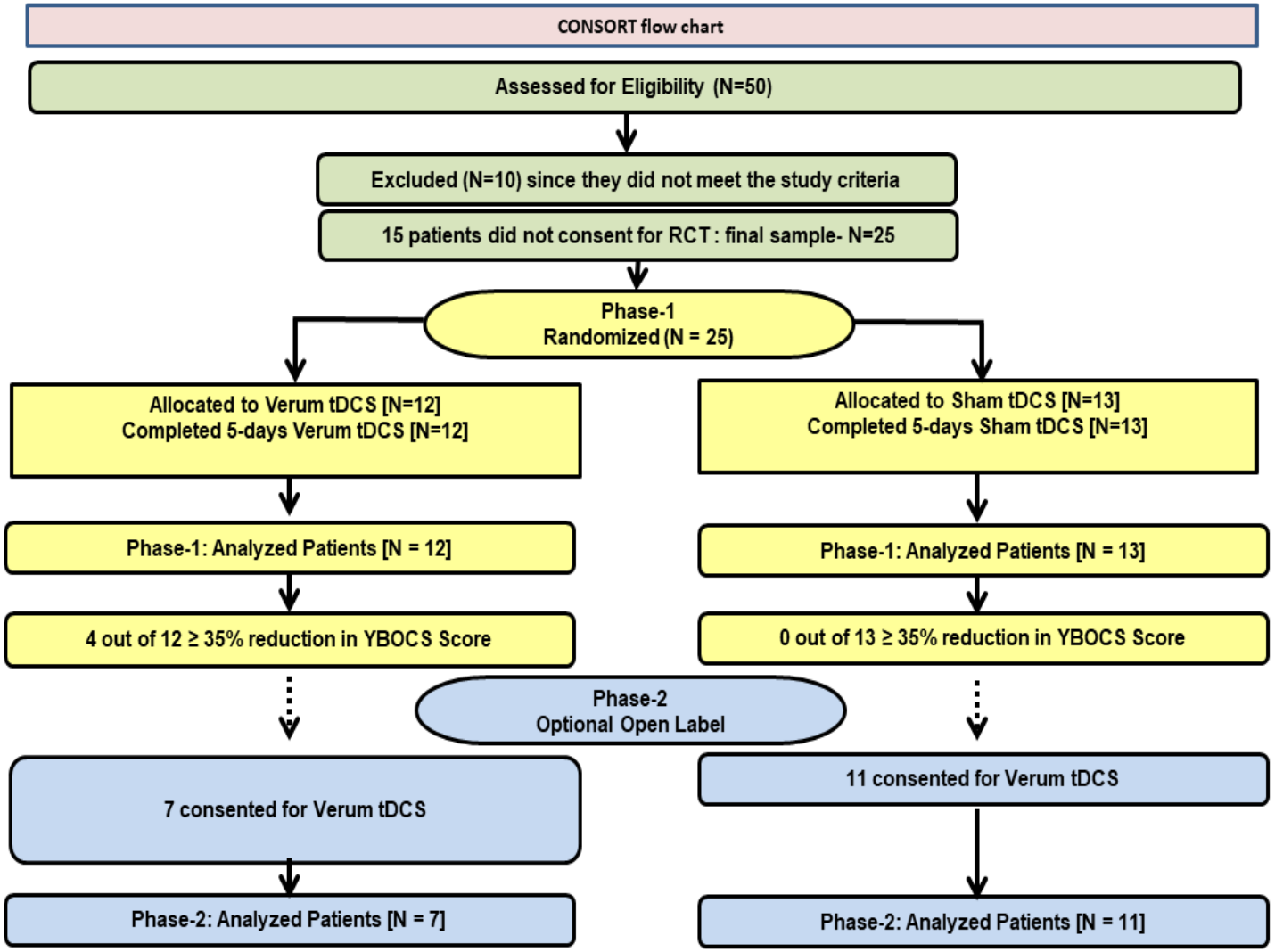
tDCS- evidence

Study	n	Anode	Cathode	Outcome
Bation et al, 2015	8	Right cerebellum	Left OFC	5/8 had ≥ 25% decrease in YBOCS scores
Mondno et al, 2015	1	Right occipital	Left OFC	26% reduction in YBOCS
Narayanaswamy et al, 2015	2	Left pre-SMA	Right supra-orbital	Around 50% reduction in YBOCS
D'Urso et al, 2015	1	Deltoid	Bilateral Pre-SMA	30% reduction in YBOCS

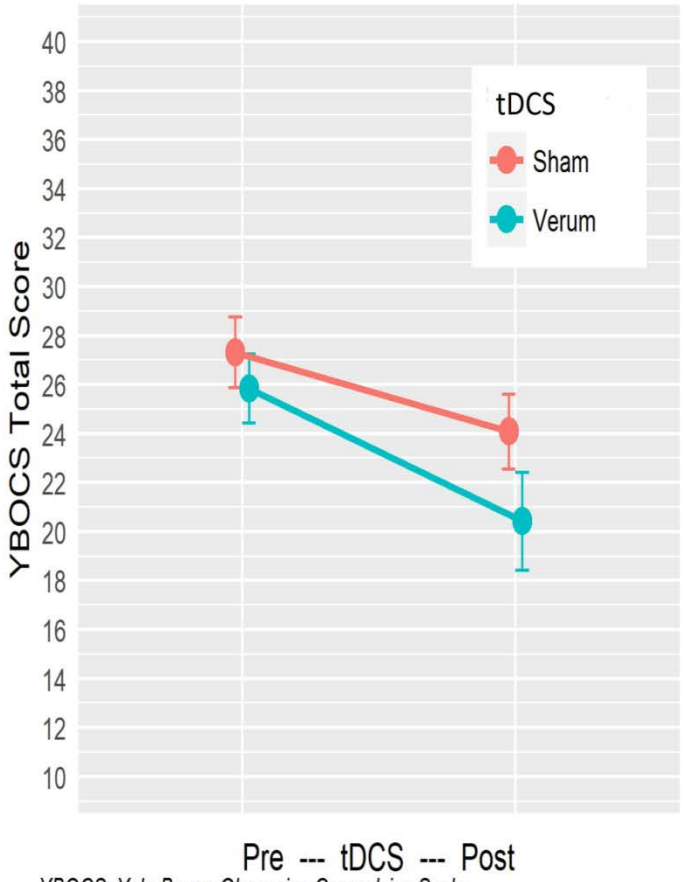
Efficacy of pre-supplementary motor area transcranial direct current stimulation for treatment resistant obsessive compulsive disorder: a randomized, double blinded, sham controlled trial

(Shayanth et al, under review in Brain Stimulation)



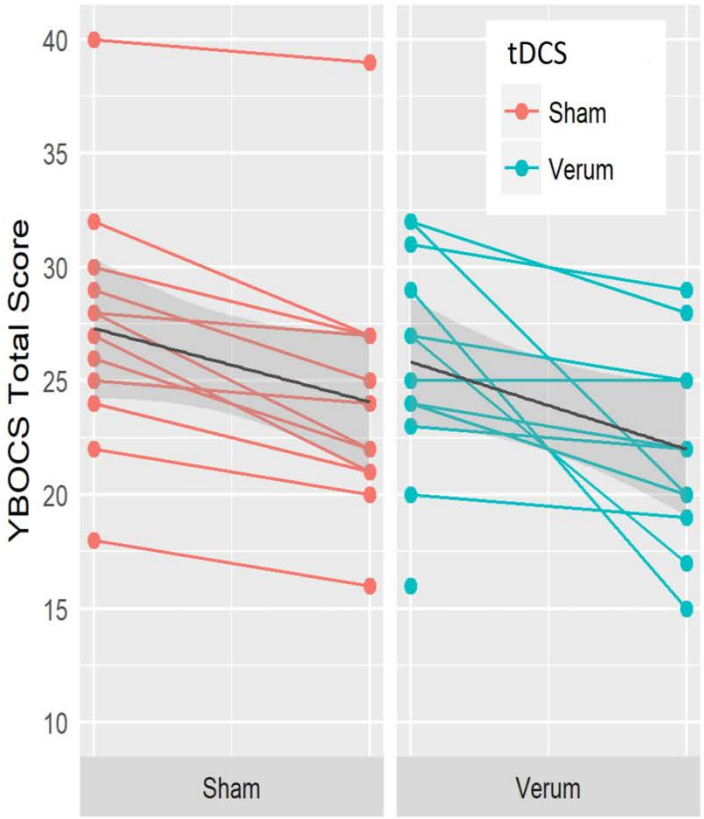


Shayanth et al., under review



YBOCS: Yale-Brown Obsessive Compulsive Scale

tDCS: Transcranial Direct Current Stimulation



YBOCS: Yale-Brown Obsessive Compulsive Scale

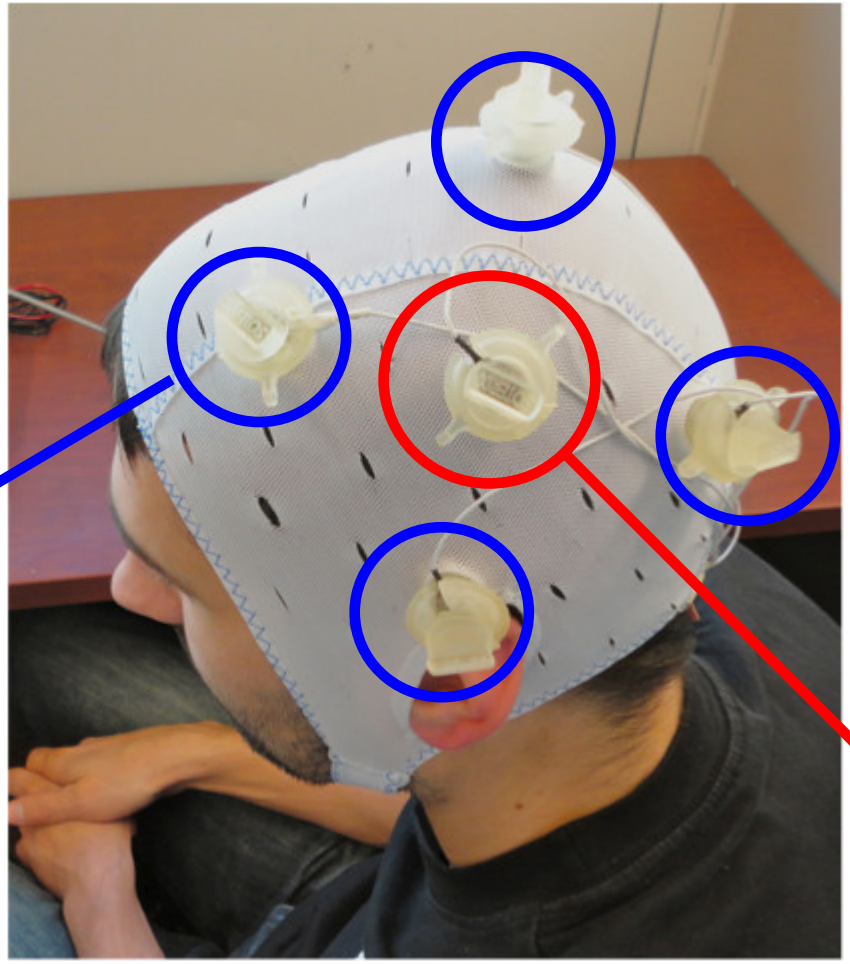
tDCS: Transcranial Direct Current Stimulation

Shayanth et al., under review

High Definition tDCS

(HD-tDCS)

- A technical enhancement over conventional tDCS
- Optimized electrodes and montages configurations
- Substantially increase in stimulation focality
- Maintains the same low intensity of current density to the brain



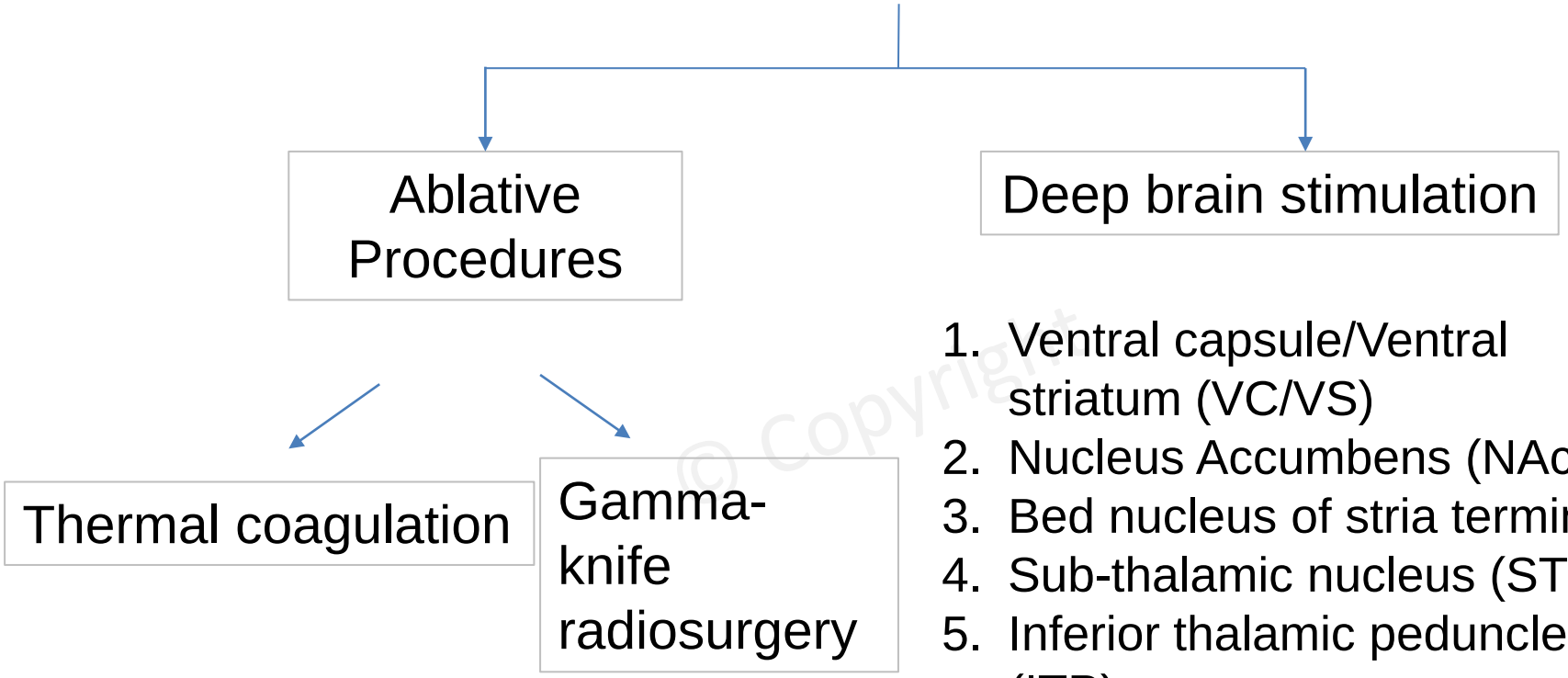
Center electrode overlying the target cortical region surrounded by **four return electrodes**

High Definition tDCS for OCD

- First-time application of add-on HD-tDCS in SSRI-resistant OCD patients
- 14 patients OCD having persistent symptoms despite adequate and stable treatment with SSRIs were administered HD-tDCS (anodal 2mA, right Pre-SMA).
- Two sessions of 20 minutes each per day, scheduled 20 minutes apart were administered for 5 consecutive days.
- There was a significant reduction in YBOCS total score after HD-tDCS sessions [Baseline vs. Post HD-tDCS= 27.6±5.7 vs. 19.4±8.0,t=3.9, p=0.002].
- **Median percentage reduction in YBOCS total score was 25.8 and there were 8 (57.1%) responders.**

(Narayanaswamy et al., manuscript under preparation)

Neurosurgical Approaches



1. Ventral capsule/Ventral striatum (VC/VS)
2. Nucleus Accumbens (NAcc)
3. Bed nucleus of stria terminalis
4. Sub-thalamic nucleus (STN)
5. Inferior thalamic peduncle (ITP)

1. **Capsulotomy**
2. **Anterior Cingulotomy**
3. Subcaudate Tractotomy
4. Limbic Leucotomy

Deep Brain stimulation

3 stages

1. Image guided insertion of electrodes (1mm) inserted

2. Subdermal implantation of neurostimulator

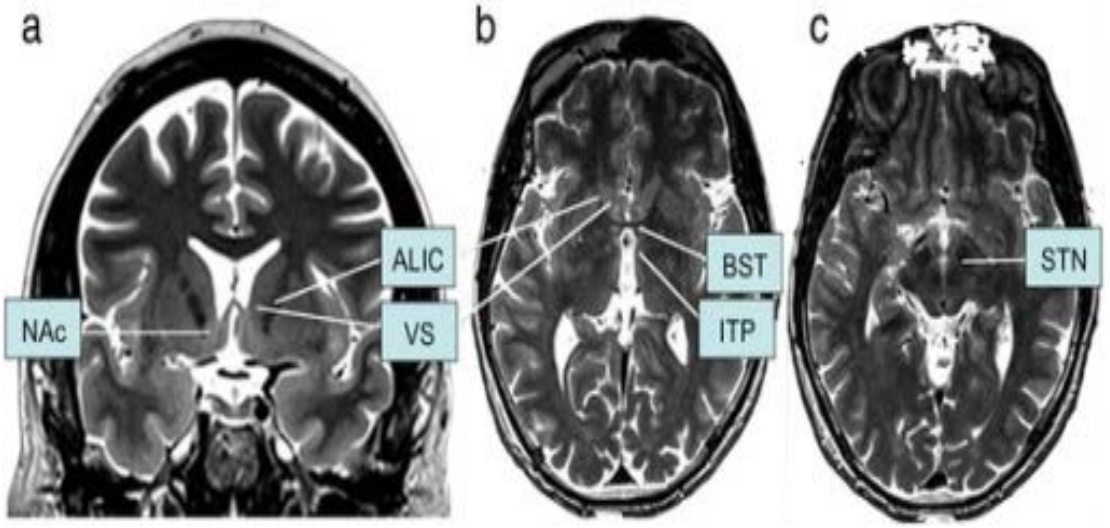
3. Programming of electrical parameters
   - Polarity, amplitude, frequency and pulse duration

Effects observed 3-6 months post-surgery

Mechanism of action

- Functional lesion
- **Disruption of dysfunctional circuits**
- Inhibiting as well as activating network effects
- Modulates oscillatory activity

Targets in OCD



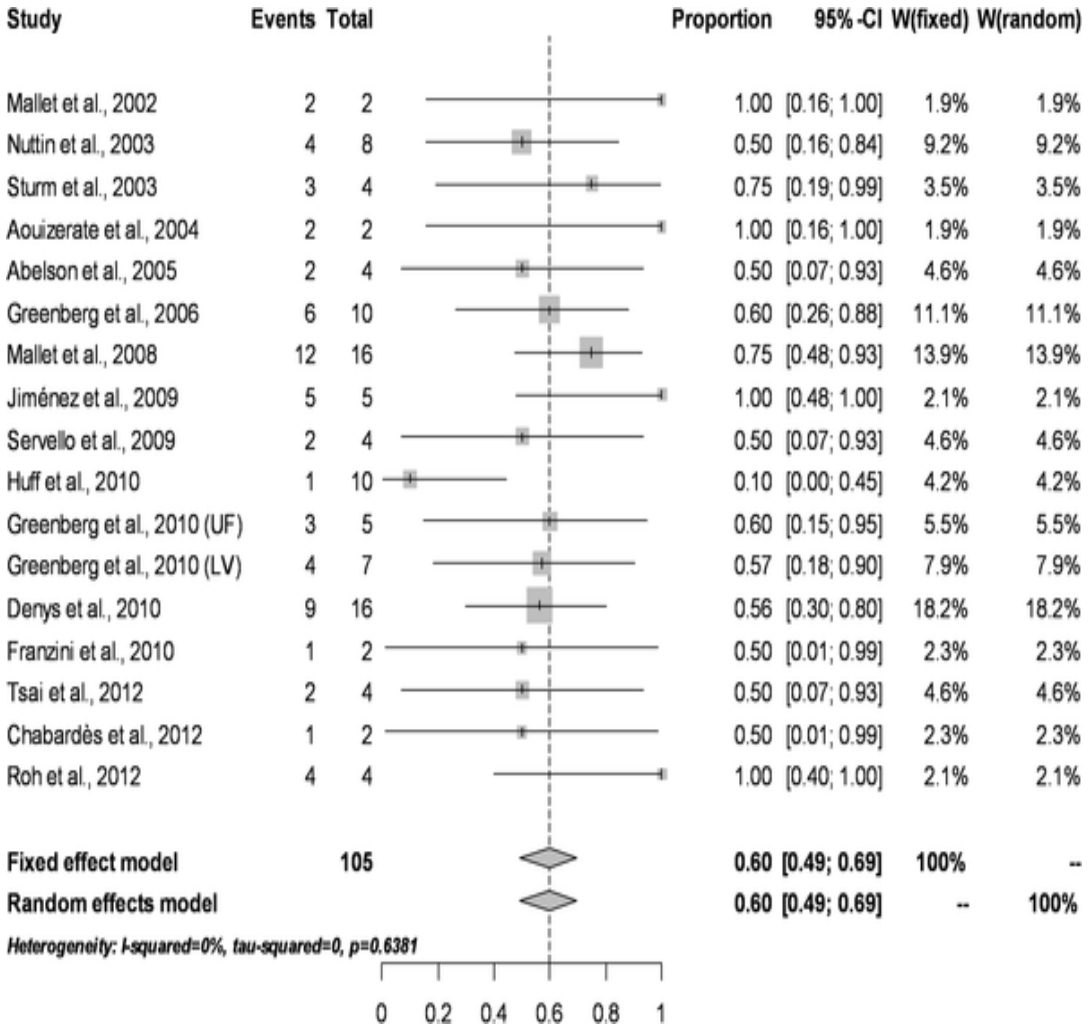
Kohl et al, 2014

- Anterior limb of the internal capsule
- **Ventral capsule/ventral striatum (VC/VS)**
- **Nucleus Accumbens**
- Bed nucleus of stria terminalis
- **Subthalamic nucleus**

Others

- Inferior thalamic peduncle

Forest Plot for percentage of responders according to standardized criteria (35% reduction in post-treatment Y-BOCS scores)



Alonso P, Cuadras D, Gabriëls L, Denys D, Goodman W, et al. (2015) Deep Brain Stimulation for Obsessive-Compulsive Disorder: A Meta-Analysis of Treatment Outcome and Predictors of Response. PLOS ONE 10(7): e0133591. https://doi.org/10.1371/journal.pone.0133591
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0133591

Summary

- Neural Circuitry Models generate potential treatment strategies
- Chronicity of compulsions seem to be producing neuroplastic changes- hence need for early interventions
- Potential utility of neuromodulation to target specific domains of symptoms (eg: Disgust)
- Role of neuromodulation to aid faster fear extinction (with CBT?)
- Psychosurgical options - DBS

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IndiaAlliance
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- ENIGMA OCD Working group

Suggested references

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