Universitat Autònoma de Barcelona

DEEP BRAIN STIMULATION AS A NEUROMODULATIVE TREATMENT FOR OBSESSIVE COMPULSIVE DISORDER

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1. Which is the ethiology of obsessive-compulsive disorder?
2. Which is the biological basis underlying deep brain stimulation applied to obsessive-compulsive disorder?
3. Is deep brain stimulation a potentially alternative treatment for obsessive-compusive disorder, a stress related pathology?
   And if so, 4. Does corticosterone play a role in this fact?

INTRODUCTION

DEEP BRAIN STIMULATION

▪Electrical stimulation of brain tissue performed directly into a desirable brain region

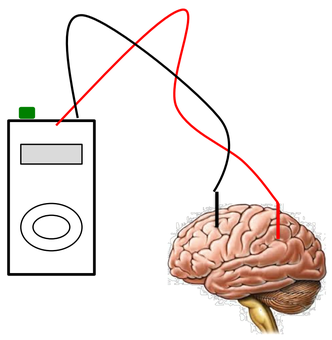


Fig.1. Scheme of deep brain stimulation

- Stimulator device
- Connector wire(s)
- Electrode(s)

OBSESSIVE-COMPULSIVE DISORDER

▪Chronic heterogeneus psychiatric disorder (2-3% worldwide)
▪Characterized by recurrent intrusive thoughts and/or repetitive compulsory behaviors

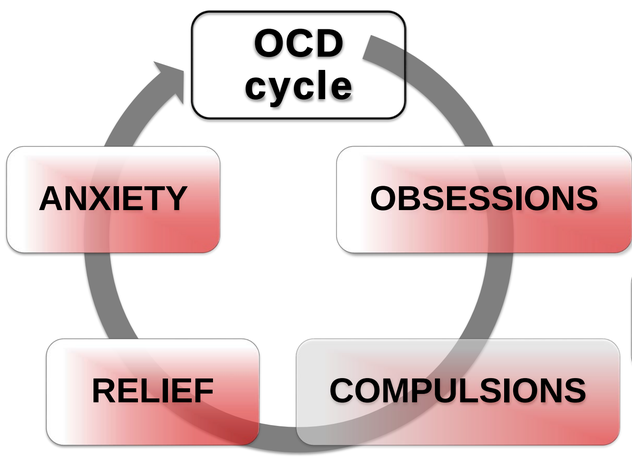


Fig.2. The OCD cycle by Calkins et. al.

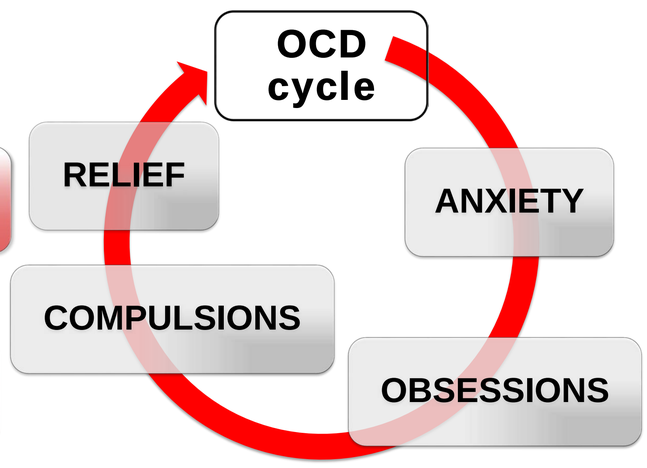


Fig.3. The OCD cycle by Anholt et. al.

Sapap3$^{-/-}$ OCD animal model

SAP90/PSD95-associated protein 3 K.O

Fig.4. Sapap3$^{-/-}$ lesions

DISCUSSION

OCD PATHOPHYSIOLOGY

Cortico-striato-thalamo-cortical pathway

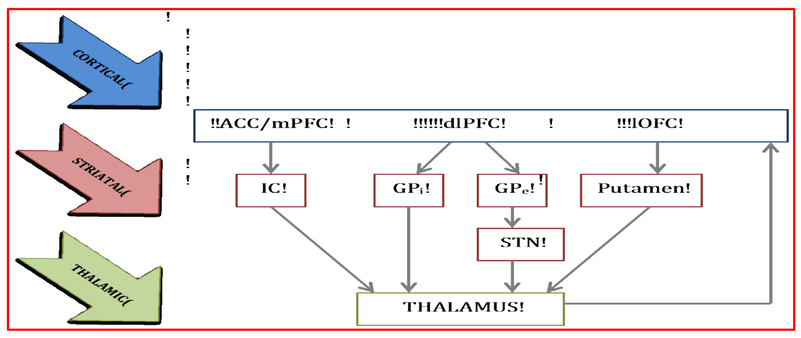
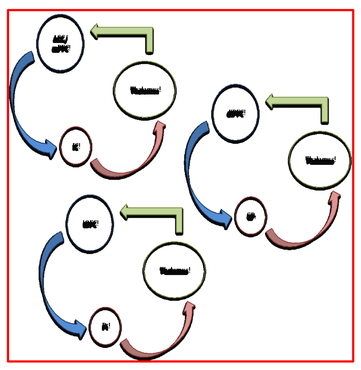


Fig.5. Schematic illustration of the cortico-striato-thalamico-cortical (CSTC) pathway implicated in the psychopathology of OCD. Abbreviations: ACC, anterior cingulate cortex; mPFC, medial prefrontal cortex; dlPFC, dorsolateral prefrontal cortex; lOFC, lateral-orbitofrontal cortex; IC, internal capsule; GP_i, internal globus pallidus; GP_e, external globus pallidus, STN, subthalamic nucleus.

Cortico-striatal loops



▪DBS normalizes NAc activity and restores intrinsic frontostriatal network dynamics
▪Border of NAc core & IC as the most effective target

Fig.6. Schematic diagrams of the cortico-striatal loops. Abbreviations: ACC, anterior cingulate cortex; mPFC, medial prefrontal cortex; dlPFC, dorsolateral prefrontal cortex; lOFC, lateral-orbitofrontal cortex; IC, internal capsule; GP, globus pallidus; Pt, putamen.

Corticosterone role in OCD

▪OCD is a stress related pathology

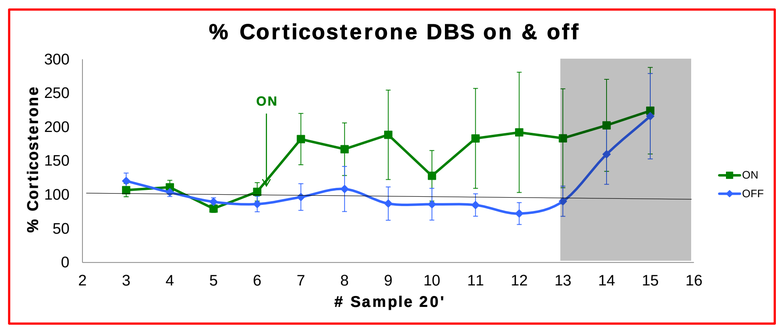


Fig.7. Corticosterone levels according to % basal levels during the time. Blue line (DBS off whole test). Green line (DBS on after sixth sample during whole test. Samples collected every 20 minutes. Shadow area corresponds to a novel cage transfer. Graphic displayed with error bars. OFF condition; statistical analysis between baseline (3-6) and after transfer (13-16) (paired t-test; 0,0303<0.05) ON condition; statistical analysis between 6/7 (paired t-test; 0,036<0,05). No effect novel cage (paired t-test; 0,739>0,05)

CONCLUSIONS

▪A malfunction of CSTC pathway is thought to be the cause of OCD
▪DBS seems to restore frontostriatal network dynamics leading to an improvement of OCD symptoms
▪DBS at IC seems to have an effect on cortical corticosterone release
▪DBS is currently under investigation, in order to elucidate some critical aspects about its working mechanism which are still unknown, stimulated by the great results already obtained

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