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Review Article

A Systematic Review on Comparison of Deep Brain Stimulation (DBS) and Transcranial Magnetic Stimulation (TMS) in the Treatment of Refractory Obsessive Compulsive Disorder (OCD)

Dhivya K*[1], Samuel Bibila[2]

[1] *Assistant Professor, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, 600097, India*

[2] *Pharm D Student, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, 600097, India*

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*Address for Correspondence:

Dr. Dhivya K, Pharm D (Ph. D), Assistant Professor, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, 600097, India

Abstract

The Diagnostic and Statistical Manual of mental disorders (DSM 4) defines obsessive compulsive disorder (OCD) as compulsive or repetitive behaviors of obsessions that a person feels driven to perform. These acts and behaviors are aimed at preventing or reducing distress but are not connected in a realistic way. OCD is a pathological hypothesis of dysfunctions occurring within the cortico-striato-thalamo-cortical loops. It is one of the most prevalent and disabling psychiatric disorder associated with decreased life quality (American Psychiatric Association). This article will provide a brief study on the comparison of deep brain stimulation and transcranial magnetic stimulation in the treatment of refractory obsessive compulsive disorder besides other pharmacological and non-pharmacological treatments.

Keywords: OCD, Deep brain stimulation, Transcranial magnetic stimulation

Introduction

OCD patients are anxious, repetitive and have ritualistic behavior provoking recurrent and intrusive thoughts or obsessions. They do unwanted things like endlessly washing hands, counting steps etc., and they also think unwantedly. Some patients think that they harm their own children and some think that deadly germs are spread by them[1].

Pathophysiology

Dysfunction of the serotonin system was postulated to be the main OCD factor. Serotonin plays a role in anxiety regulation, memory and sleep. The OCD patient's receptor sites maybe impaired or blocked, preventing serotonin from reaching its full potential.

The orbitofrontal cortex, striatum and cingulate cortex in the brain are the regions most affected[24]. Receptors like NMDA and non-NMDA (glutamate receptors), the H2, nK1, M4 are involved in OCD. 5-HT1D, 5-HT2C and opioid receptors also mediate a secondary effect.

Some receptors are negatively correlated to the OCD's severity whereas some are positively correlated. H2, nk1, M4, non-NMDA are positively correlated and NMDA, 5-HT1D, 5-HT1D, opioid and 5-HT2C are negatively correlated.

Scales used

The diagnosis is made on the measure of Y-BOCS (Yale Brown Obsessive Compulsive Scale)[22], HAM-A (Hamilton Anxiety Scale), HAM-D (Hamilton Depression rating scale), SDS work (Sheehan Disability scale domain work), SDS soc. (Sheehan disability scale domain social functioning), SDS fam. (Sheehan disability scale domain family relationships)

Total scores on the measure range from 0-40. A score of 0-7 indicates subclinical symptoms, 8-15 indicates mild symptoms, 16-23 moderate symptoms, 24-31 severe symptoms and 32-40 extreme symptoms. Subscale score for obsessions and compulsions can also be measured separately.

Treatments

Pharmacotherapy and Cognitive Behavioral Therapy (CBT) are effective but they have their limitations[25]. Pharmacotherapy has side effects such as anxiety which cause 25% patients to drop out. CBT has only partial response. 10% of patients do not respond and are severely affected. Therefore, high risk of

disability and morbidity are accompanied[3]. The common comorbidity of OCD is the major depressive disorder leading to high suicide rate. In fact, 25% of OCD patients will attempt for suicide[13]. The current first line medicines are high doses of Serotonin Reuptake Inhibitors (SRI's) or Clomipramine and psychological social treatment. Cognitive Behavioral Treatment is an asset and time escalated treatment. An assorted exhibit of anti psychotics has been utilized in the treatment but its long-term use leads to metabolic unfavorable effects restricting its utilization[21].

In the last decades, Deep Brain Stimulation (DBS) and Transcranial Magnetic Stimulation (TMS) are introduced for the treatment of refractory OCD[15].

Deep Brain Stimulation (DBS)

It is one of the most successful treatment for many neurological diseases[1]. Nuttin et al published that DBS can be used as an anterior capsulotomy[13] in OCD producing 50% improvement anterior in its symptoms[8]. DBS directly stimulates the target within the brain.

Features

The technique alters the function of neural pathways[11]. DBS targets the internal capsule towards the anterior limb and also the subthalamic nucleus, ventral striatum, the nucleus accumbens, the inferior thalamic peduncle[19].

It involves the appliance of electrodes in the brain[30]. Both the hemispheres are stimulated in the target area. Four electrodes are present in each lead, connected to the battery through the wire placed in abdomen or clavicle subcutaneously. The activity of the electrode is programmed externally through telemetry with a portable appliance communicating with the pulse generator. The anatomic reach of stimulation area is adjusted by stimulating the electrodes separately. Pulse, frequency, and intensity are programmable. The frequencies vary between 2-185Hz. It ranges between 60-150ms for pulse widths, current power lies between 0-10V.

Improvement in obsessions and compulsions occur within days to weeks. The response is preceded with a rapid mood elevation or hypomania[8]. It also improves cognitive functions in OCD patients.

Procedure

The head frame is placed on head (known as streotactic head frame) before the surgery to keep the head still during brain imaging. The frame is secured to the head using surgical pins or screws. MRI is used to identify the area where the electrodes should be placed. Local anesthetic is given during the procedure. The deep brain stimulation system will be implanted by the neurosurgeon in two stages.

1. Brain Surgery:

The surgeon places a thin wire lead with electrodes into specific brain areas. The pulse generator is implanted near the collarbone. It is connected to the electrodes by means of a thin wire running under the skin.

2. Chest wall surgery:

It is the second stage of implantation in which the pulse generator near the collarbone will be programmed to send continuous impulses. The patient can turn it on and off when required using special remote control.

Mechanism

The exact mechanism is unknown but there are two hypotheses.

- DBS causes a functional lesion by inhibiting the brain core that is stimulated. It is caused by depolarization blockage of neurons due to synaptic depression (exhaustion) or by synaptic inhibition via neuronal jamming that activates a meaningless pattern.
- DBS activates the neuronal network that is connected to the brain core. This activation leads to modulation of the pathological neuronal network activity.

The therapeutic effect of DBS is due to the combination of indirect and direct effects on the stimulated brain. The neurons are influenced in different ways in centre of the stimulation area. Hence, the neuronal cell body is probably restrained. This restores intrinsic brain network dynamics and normalized nucleus accumbens activity.

Advantages

1. Decreased anxiety.
2. Improved mood.
3. Diminished OCD symptoms.
4. It does not eliminate the need for ongoing medication management and behavior therapy.
5. It is a standard treatment option in patients who haven't shown any improvement in other treatment methods.
6. The method is potentially reversible incase of discomfort or problem. (ie.,) It can be removed or turned off[11].

Disadvantages

1. Unintended cessation occurs on a regular basis.
2. High currents are used in the treatment leading to battery depletion every 1-2 years[18].
3. When battery is depleted, and the stimulation is abruptly stopped, there is worsening of psychiatric conditions.
4. The increase in anxiety and decreased alertness after cessation leads to OCD symptom relapse[11].
5. During acute stimulation, patients may have side effects such as increased mood, decreased anxiety, paresthesis, visual changes, irritability and facial muscle movements.

Trans cranial Magnetic Stimulation (TMS)

It is a non-invasive technique that activates and modifies the neuron activity involving depolarization or hyper polarization in the axon of the neurons.

Features

The procedure uses electromagnetic induction to induce weak electrical currents by rapidly changing the magnetic field which in turn causes electrical current on specific brain parts[7]. It is of interest in non-compliance, pharmacological treatment failure etc. It is also an option for refractory OCD[15].

Types

1. Deep Trans cranial Magnetic Stimulation (dTms)
2. Repetitive Trans cranial Magnetic Stimulation (rTms)

Comparison: TMS and rTms

TMS produce a single pulse resulting in short responses whereas rTMS is the repetition of electromagnetic stimulations that produce repeated pulses having prolonged effects in the brain[21].

Repetitive Trans cranial Magnetic Stimulation

Procedure

It is a novel, safe technique using repetitive, brief, intense magnetic fields generated by a coil placed over the scalp that produces electric field in the underlying brain regions through electromagnetic induction. Low frequency rTms alters the activity of orbitofrontal cortex region (OFC)[19].

rTms results in lasting metabolic activity changes to the stimulation sites and connected distant sites. It may modulate neural networks which are implicated in OCD. The cortico-striato-thalamo-cortical circuits are associated with OCD pathophysiology. These may include affective circuit, dorsal cognitive circuit, sensorimotor circuit and ventral cognitive circuit. Communication between these networks are associated with functions like habits, reward learning and compulsivity[5]. Normalizing these network activities may give relief in OCD. It may also identify the predictors of non-response like the presence of sleep disturbances etc[23].

The frontostriatal circuits especially the anterior cingulate cortex and orbitofrontal cortex are associated with OCD pathophysiology. Low frequency stimulation less than or equal to 1Hz may decrease[29] and high frequency stimulation greater than or equal to 5Hz increases cortical excitability of 2-3 cms region below the scalp. However, the anterior cingulated cortex, orbitofrontal cortex, caudate, putamen etc., are not accessible for rTMS stimulation. Hence they are indirectly modulated through stimulation of the superficial cortical regions that are inter connected.

Dorsolateral Prefrontal Cortex (DLPFC) and Supplementary Motor Area (SMA) are accessible through regular TMS coils and have deep connections with basal ganglia[1].

Sessions

Complete treatment of OCD may need upto 3 courses of sessions. They may take place over 3-6 weeks. Each session won't be longer than 30 minutes.

Features

The procedure alters the neural activity and excitability in the targeted brain regions. It can be excitatory or inhibitory. This is the important rationale of rTms. The brain state dependent modulating effects acts as a parameter affecting rTms.

By this factor, the treatment outcomes maybe improved in patients who develop treatment resistance and increased illness[8].

Advantages

1. It uses magnetic coil to stimulate brain.
2. Patient can remain fully alert and awake during treatment.
3. Patients can return to their daily activities immediately after treatment sessions.
4. TMS is a promising and a more effective treatment method for OCD.
5. TMS is 2-3 times more effective than antidepressants in OCD treatment.
6. The side effects are minimal. The common ones are slight headache, twitching, spasms, neck pain, facial pain, jaw pain, muscle pain. But it goes away throughout the course of treatment.

Methodology

Study design

Systematic review

Aim

To compare deep brain stimulation and trans cranial magnetic stimulation in the treatment of refractory OCD patients.

Objective

1. To compare the safety and effectiveness of deep brain stimulation and trans cranial magnetic stimulation in OCD patients.
2. To detect adverse effects after the treatment.
3. To ensure the mean age of the treatments.
4. To compare the usefulness of the two treatments on OCD refractory patients.

Need for the study

- To find out which treatment among DBS and TMS will effectively alleviate symptoms of OCD refractory patients.
- To measure safety concerns between DBS and TMS techniques.
- To study the adverse effects of these long term treatments.
- To distinguish between DBS (invasive) and TMS (non-invasive) methods.
- To find out the majorly used diagnostic scale for the treatment of refractory OCD patients.

Search strategy

Systematic search in the Cochrane library, PubMed, Science direct electronic databases for studies that compared between DBS and TMS in refractory OCD. The included studies were published from 2005-2020. The search terms included are DBS in OCD patients and TMS in OCD patients. We did not find other studies in this manual search. Screening the reference list of included studies in their related websites was also done.

Inclusion and Exclusion criteria

Inclusion

1. Type of study: Retrospective study, randomized controlled clinical trial, prospective study on DBS and TMS treatment on OCD patients.
2. Age : 18-68 years
3. Minimum illness duration : 2 years
4. Gender : Male and female
5. Patients who are refractory to atleast two treatment sessions with pharmacotherapy and CBT.
6. Y-BOCS score greater than 16

Exclusion

1. Certain publications like reviews, manuscripts, conference abstracts, pilot studies, comments and editorials.
2. Studies with replicated and insufficient data.
3. Preclinical studies.
4. Studies published in non-english language.
5. Pregnancy, child bearing age, substance abuse, alcoholics, breast feeding, neurological disorder, suicidal risk, psychiatric issues other than OCD.

Outcomes analyzed

- ✓ The primary outcome was to compare the responses showed by refractory OCD patients after DBS or TMS treatment.
- ✓ Using the scores showed from Y-BOCS scale, the responders and non-responders were distinguished.
- ✓ The secondary outcome was to find out the adverse effects of DBS and TMS treatments.

Selection of studies for inclusion and data extraction

The search results were combined and duplicates were removed. Screening was done based on title and abstracts for relevance at first and then the full text was reviewed. Next, complete and careful article reviews were done to confirm those studies which described the response from DBS or TMS in the treatment of refractory OCD patients.

The studies that met the inclusion criteria were considered eligible for this systematic review.

Results

A total of 801 studies were identified (419 in Elsevier, 2 in Cochrane library, 380 in PubMed). 443 studies were excluded after reading the titles and abstracts. 102 studies were removed because they were not specific with OCD. Some others were excluded because they did not have data (n=47), some were not published in English language (n=62), manuscripts (n=41), insufficient data (n=43) and pilot study (n=51). Finally, 12 studies met the criteria and were included in the present study.

Summary of the included studies

S.No.	STUDY TITLE	AUTHOR	OBJECTIVES	RESULTS / CONCLUSION
1.	Cognitive Behavioral Therapy augments the effects of DBS in OCD	M. Mantione et al	CBT could optimize post operative management in DBS. Evaluation of CBT efficacy as deep brain augmentation was done targeted at nucleus accumbens	A combined treatment of DBS and CBT may be optimal for improving OCD symptoms in refractory patients
2.	Rapid effects of DBS reactivation on symptoms and neuroendocrine parameters in OCD	PP de Koning et al	To evaluate rapid clinical changes (OCD, anxiety, mood) on DBS. To assess various other neuroendocrine parameters that are related to hypothalamic pituitary axis and their DBS association which induced rapid clinical changes.	After 1 week of DBS discontinuation, reactivation results in a rapid, simultaneous +/- improvement of anxiety, depression and OCD symptoms in 8 out of 10 initial DBS responders.
3.	Three year outcomes in DBS for highly resistant OCD	BD Greenberg et al	To examine outcomes of DBS over 3 years in patients with severe treatment resistant OCD	Ventral capsule or ventral striatum site (VC/VS) has encouraging therapeutic effects on DBS
4.	Six nine year follow ups of DBS for OCD	Sarah M Fayad et al	To establish long term safety and effectiveness of DBS of VC/VS for adults with OCD	Reduction in OCD symptoms. Secondary outcomes excluded depressive symptoms which was increased over the follow up period. Qualitative feedback indicated DBS was well tolerated by subjects
5.	DBS for OCD : Long term analysis of life quality	Ooms P et al	To determine to what extent DBS affects QOL over a period of atleast 3 years. To investigate whether the symptom improvement correlates with QOL improvement	Patient's QOL improved in general score and in 3 of 4 WHOQOL-BREF domains. It suggests that the improvement caused by DBS is not limited to symptom reduction alone but also has a positive influence on patient's perception of their physical, psychological, environmental and global QOL
6.	DBS of nucleus accumbens for treatment of refractory OCD	Damiaan Denys et al	To determine whether bilateral DBS of nucleus accumbens is an effective and safe treatment for refractory OCD	Depression and anxiety decreased except for mild forgetfulness and word finding problems. No permanent adverse effects were reported. Bilateral DBS maybe an effective and safe treatment for refractory OCD.

7.	rTms improves symptoms and reduces clinical illness in patients suffering from OCD – results from a single, blind, randomized clinical trial with sham crossover condition	M. Haghhighi et al	To test the hypothesis that rTms improves symptoms and resuces illness severity in patients suffering from treatment resistant OCD	Both self and expert reported symptom severity reduced as compared to sham condition. Full and partial responses were observed in rTms but not in sham. This suggests that rTms is a successful intervention for patients who suffer from treatment resistant OCD
8.	The effect of low frequency rTms at orbitofrontal cortex in the treatment of patients with medication refractory OCD-A retrospective open study	Kumar et al	To assess the safety and effectiveness of low frequency rTms (LF-rTms) over left orbitofrontal cortex (Lt-OFC) as a potential augmentation strategy in the treatment of patients with medication refractory OCD in a real world clinical setting. To examine the factors affecting response to rTms and durability of effects produced by rTms over 1 month of follow up period	There was a decrease in mean Y-BOCS scale at the end of 20 sessions of rTMS compared with baseline (7.04 +/- 5.07; P<0.001) with no changes further during subsequent 1 month follow up period. High number of failed medication trials was found to be associated with non responses to rTMS treatment
9.	Sleep disturbances in OCD – Association with non response to rTms	L. Donse et al	To compare sleep disturbances between OCD patients and healthy subjects and between rTMS responders and non responders. To determine sleep related predictors of rTMS non response	Sleep disturbances were more prominent in OCD patients than in healthy subjects. The OCD group consisted of 12 responders and 10 non responders. The CRSD model accurately predicted non response with 83% sensitivity and 63% specificity whereas the insomnia model did not. CSRD may serve as a biomarker for different subtypes of OCD
10.	Efficacy and clinical predictors of response to rTMS in pharmacoresistant OCD-A retrospective study	Rostami et al	To investigate the efficacy of rTMS over two potentially involved cortical regions (ie) SMA and DLPFC for reducing OCD symptoms. To identify clinical and demographic predictors that distinguish between rTMS responders and non responders in OCD	Patient's scores in Y-BOCS and Beck anxiety / depression inventories were decreased following rTMS treatment. There were no difference between response rates of patients in DLPFC and SMA groups. The factors "obsession severity", "resistance", "disturbance", "interference due to obsessions" and "resistance against compulsions" of Y-BOCS responded to rTMS
11.	Efficacy and safety of deep TMS for OCD-A prospective multicenter randomized double blind placebo controlled trial	Carmi et al	To report results of a prospective multicenter randomized double blind study in which outcomes of dTMS targeting mPFC and Anterior Cingulate Cortex (ACC) were compared with those of sham stimulation	High frequency dTMS over medial prefrontal cortex and ACC improved OCD symptoms and maybe considered for patients who do not respond to pharmacological and psychological interventions
12.	Use of EEG for predicting the treatment response to TMS in OCD	Metin et al	To assess the predictive power of quantitative EEG (qEEG)for the treatment response to right frontal TMS in OCD using a machine learning approach	Among four EEG bands, theta power successfully discriminated responsive from non-responsive patients. Responsive patients had more theta powers for all electrodes as compared to non responsive patients.

Study and patient characteristics

12 eligible studies were conducted in America, Europe, India and Germany. A total of 357 participants with a mean age of 38.2 years, range varying between 28-68 years were included with the majority of females. The treatments used was DBS and TMS. All studies were in English language. Two studies were multicenter trials. Average follow up evaluation was 2.9 years ranging from 1-9 years.

CHARACTERISTICS	NUMBER OF STUDIES	NUMBER OF PATIENTS
Total	12	357
Gender		
Male	12	137
Female	12	220
Age (mean)	12	38.3 years
Treatment		
DBS	6	80
TMS	6	277
Diagnostic tool		
Y-BOCS	12	322
HAMILTON-A	4	63
HAMILTON-D	6	158
Study design		
Prospective	7	190
Retrospective	3	140
RCT	1	21
Descriptive	1	6
Follow up (mean)	12	2.9 years
Publication year		
2006-2009	1	10
2010-2015	4	69
2016-2020	7	278
Comorbidities		
Major depressive disorder	5	68
Panic disorder	2	2
Dysthymia	2	2
Depression	1	22
Study location		
America	3	115
Europe	7	157
India	1	25
Germany	1	65

Responders and non-responders in DBS and TMS

The summary of responders and non-responders observed in DBS :

SOURCE / YEAR	TOTAL NUMBER OF PATIENTS	RESPONDERS	NON-RESPONDERS
M. Mantione et al 2014	16	9	7
PP de Koning et al 2016	15	10	5
BD Greenberg et al 2006	10	8	2
Sarah M Fayad et al 2016	6	4	2
Ooms P et al 2013	16	After 8 months of treatment:9 After 3 years of treatment:11	After 8months : 7 After 3 years : 5
Damiaan Denys et al 2010	16	9	7

The summary of responders and non-responders observed in TMS:

SOURCE / YEAR	TOTAL NUMBER OF PATIENTS	RESPONDERS	NON-RESPONDERS
M. Haghighi et al 2015	21	Full response : 9 Partial response : 2	10
Kumar et al 2017	25	13	12
L. Donse et al 2017	22	12	10
Rostami et al 2020	65	30 **Active treatment** Full response : 19 Partial response : 25 **Sham treatment** Full response : 8 Partial response : 19	35 **Active treatment** Full non-response : 23 Partial non-response : 17 **Sham treatment** Full non-response : 37 Partial non-response : 26
Carmi et al 2019	Active treatment : 42 Sham treatment : 45		
Metin et al 2019	50	32	18

Summary of adverse effects of DBS studies :

SOURCE	ADVERSE EFFECTS
BD Greenberg et al 2006	Transient sadness
	Anxiety
	Euphoria
	Giddiness
	Jaw muscle tightness associated with dysarthria
	Physical sensation of sadness
	Chemical or metallic smell of flushing
Sarah M Fayad et al 2016	Insomnia
	Sleeping too much
	Shooting tingling on right side of the body
	Metal taste and jaw clenching
	Mild skin redness and burning on head and chest
Damiaan Denys et al 2010	Wound infection at incision
	Tiredness
	Nausea
	Feeling numbness at incision
	Headache
	Hypomanic symptoms
	Cold shivers
	Stomach aches
	Dizziness
	Taste reduction
	Itch on right arm
	Less blood flow during menstruation
	Allergy
	Sneezing
	Difficulty falling asleep
	Micturition problems
	Forgetfulness
	Paraesthesias in hands or feet

Summary of adverse effects in TMS studies:

SOURCE	ADVERSE EFFECTS
Kumar et al 2017	Headache
	Localized scalp discomfort
Rostami et al 2020	Occassional headache
	Dizziness
Carmi et al 2019	Headache
	Significant suicidal thoughts

Discussion

This study is a compilation of the characteristics [(ie) total population, gender, age, types of treatment, diagnostic tools, study design, follow up, publication year, co-morbidities, study location] of responders and non-responders from DBS and TMS. It also includes the adverse effects occurred due to DBS and TMS from the 12 included studies. The primary objective of the study was to compare the effectiveness of DBS and TMS based upon the responses showed from refractory OCD patients. The other objectives of this study was to compare the non-responders and adverse effects due to DBS and TMS.

OCD occurs in 2-3% of the total population. It is a psychiatric disorder in which patients suffer from either obsessions or compulsions or both[12]. Obsessions refer to recurrent and persistent thoughts, images or impulses that are inappropriate and intrusive causing distress or anxiety. The anxiety arising due to obsessions lead to compulsions[1]. It is referred as behaviors that are repeated by the person or mental acts that are driven to perform[1].

The standard treatment involves the combination of medication and / or psychotherapy. Primary treatment includes both Selective Serotonin Reuptake Inhibitors (SSRI's) like fluoxetine, fluvoxamine, paroxetine, sertaline, citalopram, escitalopram and CBT. Clomipramine is a tricyclic antidepressant and it primarily acts as an SSRI[11]. Apart from this, neurosurgical treatments are also available. The patients who does not show any response from these treatments are known as refractory OCD patients[11]. The effects of the treatment are assessed with psychopathological scales which measure number of symptoms. (ie) Y-BOCS, HARS, HDRS[12].

DBS delivers electrical activity of short-high frequency pulses[9]. The process involves implantation of electrodes in brain that produces a continuous electric pulse to modulate the specific brain areas. Leads are connected to a battery through a wire placed below clavicle or in abdomen subcutaneously. Frequencies for varying stimulation parameters are between 2-185Hz for pulse widths between 60 and 150ms for the current power between 0 and 10V[1]. Most patients are stimulated in the nucleus accumbens area[12]. The main advantage of the technique is that the effect is reversible and the stimulation parameters are adjustable[10]. It is effective in 57% of OCD patients[12].

TMS is a non-invasive technique that activates and modifies action of neurons. rTMS uses electromagnetic induction to induce weak electrical currents through rapidly changing magnetic field that produces electrical current in general or specific brain areas. The difference between TMS and rTMS is the repetition rate of electromagnetic stimulations. Single pulse of TMS generate short responses[26] and repeated pulses give prolonged effects in brain[19].

From the total of 12 studies included, 6 discussed about responders and non-responders after DBS treatment and other 6 about responders and non-responders after TMS treatment.

The effectiveness of DBS treatment:

- ✓ M. Mantione et al study showed 9 responders and 7 non-responders among 16 patients.
- ✓ PP de Koning et al study showed 10 responders and 5 non-responders among 15 patients.
- ✓ BD Greenberg et al study showed 8 responders and 2 non-responders among 10 patients.
- ✓ Sarah M Fayad et al study showed 4 responders and 2 non-responders among 6 patients.
- ✓ Ooms P et al study showed 9 responders after 8 months of treatment, 11 responders after 3 years of treatment and 7 non-reponders after 8 months of treatment, 5 non-responders after 3 years of treatment among 16 patients.
- ✓ Damiaan Denys et al study showed 9 responders and 7 non-responders among 16 patients.

The effectiveness of TMS treatment:

- ✓ M. Haghighi et al study showed 9 full responders, 2 partial responders and 10 non-responders among 21 patients
- ✓ Kumar et al study showed 13 responders, 12 non-responders among 25 patients.
- ✓ L. Donse et al study showed 12 responders and 10 non-responders among 22 patients.
- ✓ Rostami et al study showed 30 responders and 35 non-responders among 65 patients.
- ✓ Carmi et al[28] study showed 19 full responders, 25 partial responders, 37 full non-responders, 26 partial non-responders, from Sham treatment among 45 patients.
- ✓ Metin et al study showed 32 responders and 18 non-responders among 50 patients.

The adverse effects of DBS from the studies:

- Transient sadness
- Anxiety
- Euphoria
- Giddiness
- Jaw muscle tightness with dysarthria
- Physical sensation of sadness
- Sad mood
- Chemical or metallic smell
- Flushing
- Metal taste
- Mild skin redness
- Wound infection at incision
- Headache
- Hypomanic symptoms
- Stomach aches
- Taste reduction
- Less blood flow during menstruation
- Difficulty falling asleep
- Paresthesia in hands or feet
- Sleeping too much
- Insomnia
- Shooting tingling on right side of the body
- Jaw clenching
- Burning on head and chest
- Tiredness
- Nausea
- Feeling numbness at incision site
- Cold shivers

- Dizziness
- Itch in right arm
- Allergy
- Sneezing
- Micturition problems
- Forgetfulness

The adverse effects of TMS treatment from three studies are

- Headache
- Localized scalp discomfort
- Occassional headache
- Dizziness
- Significant suicidal thoughts

Conclusion

When comparing the responders between DBS Vs TMS, it was found as 75% of responders from DBS and 61% responders from TMS, so the non-responders were 25% in DBS and 39% in TMS. When comparing the adverse effects between DBS Vs TMS, it was found that DBS showed more adverse effects than TMS. According to age DBS treatment had more geriatrics patients when compared to TMS treatment. Limitations of this study were, there are no studies revealed about the cost for these treatments and studies that shows about the adverse effects are less. These studies consists of relatively small number of patients so, we suggest that the results need to be validated through larger sample size in the future studies and more studies should be conducted to find out the adverse effects. Expert clinical skills are required to evaluate how OCD symptoms change over time.

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