Special Article

Resurgence of Psychosurgery: Modern Neurosurgery for Mental Disorders

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Background: *A significant percentage of psychiatric patients fail all treatment modalities including drugs, psychotherapy and electroconvulsive therapy. Modern psychosurgery is a viable option in these patients. Also the history of psychosurgery is very interesting and still influencing public perception nowadays.*
Objective: *The surgery aim to improve disabling symptoms of patients with minimal complications.*
Material and Method: *Medical literatures were reviewed by the authors regarding history, surgical procedures and results.*
Results: *Once almost extinct, psychosurgery now becomes more important therapeutic role for treatment of psychiatric diseases. Improved neurosurgical techniques led to significant drop in morbidity and mortality. Although not perfect, better understanding of pathophysiology also led to more precise target for therapy with hopefully more efficacy. Recently, there is trend toward reversible neuromodulation instead of ablative procedures. For psychiatric diseases, such as obsessive compulsive disease and major depressive disorder, substantial numbers of patients fail combination of standard treatments: drugs, psychotherapy and electroconvulsive therapy which have grave prognosis. The need for effective therapy and advanced in knowledge in this field will lead to expanded use of psychosurgery in the near future.*
Conclusion: *History of psychosurgery is reviewed. Principle of pathophysiology, patient selection processes and perioperative management are described. Surgical procedures both ablative surgery and neuromodulation are demonstrated as well.*

Keywords: *psychosurgery, psychiatric disorder, stereotactic surgery*

J Med Assoc Thai 2017; 100 (Suppl. 2): S186-S195
Full text. e-Journal: *http://www.jmatonline.com*

Mental disorders are major health problem worldwide. The World Health Organization (WHO) estimates that 5 of the top 10 causes of disability worldwide are disorder in the mental and behavioral disorder category and causing 7.4% of global disability-adjusted life years (DALYs) loss[1]. About nearly one-third of depressive patients and 10% of obsessive-compulsive patients will become resistant to all modalities of standard treatments[2,3]. These patients have poor prognosis and leading to seek for novel treatment. Psychosurgery as a treatment for mental disorders has a long, interesting history since ancient time. Once nearly exterminated because of indiscriminate usage, it is increasingly used worldwide due to advancement of surgical techniques and understanding of the diseases.

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History

Ancient period

Attempts to treat psychiatric disease were found since very long time. Trepanation (drilling a hole through the skull) was found in buried skulls from Europe, North Africa and South America, dated back to about 5,000 years ago[4,5]. In Greece period, Hippocrates and Galen mentioned of trepanation. Also, there were evidences of trepanation in Renaissance period[4,5].

Early period

In the 19th century, knowledge of functional brain area was developed from clinical cases. Studies from survivors of brain injuries and brain lesions helped scientists to understand functions of specific brain areas. Localization also expanded from neurophysiolocal studies from animal experiments[4,5]. Based on these ideas, Burckhardt, a Swiss psychiatrist, performed topectomies on six patients with intractable psychiatric illness by himself. Most patients had aggression and response was about half. After bad criticisms, he stopped his experiment[6]. Puusepp,

Estonian neurosurgeon, tried to disconnect the frontal and parietal lobe in 3 patients with affective disorders, but the procedure was not successful[7].

In 1930s, John Fulton, American neuroscientist, studied the effects of frontal lobe resection in primates by observation of animals' behavior after removing parts of the brain. In 1935, at the Second International Neurologic Congress in London, Fulton and Jacobsen reported the result of bilateral frontal lobes resection in two chimpanzees which showed less emotions and also less anxiety when failed the experimental tasks[8].

At that time, there were few treatments available for psychiatric illness. Hospitals and asylums were overwhelmed with psychiatric patients[4,5]. New promising treatment could be rapidly accepted. In 1935, Egas Moniz, a Portuguese neurologist, inspired by Fulton's work, performed the first frontal lobotomies along with his neurosurgeon colleague, Almeida Lima. Initially, they used alcohol injection and laterinvented the leukotome instrument for more precise operation and reported series of 20 leukotomies. The term "psychosurgery" was used first by Moniz[4,5,9].

Inspired by Fulton and Moniz, Walter Freeman, American neurologist, performed the first frontal lobotomy in USA at 1936. Freeman and his neurosurgeon colleague, James Watts, worked together and reported their first 200 lobotomy cases which had substantial improvement but also significant negative outcomes,including deaths[4,5,10]. To obliterate the need for surgeon and anesthetist, Freeman later developed transorbital technique for lobotomy by using sharp instrument "ice-pick" orbitoclast[11]. Freeman then traveled across USA and popularized this technique. About 60,000 lobotomies were performed in USA and Europe in rather non-specific indications. This crude technique combined with bad patient selection led to stigmata of psychosurgery in general perceptions until nowadays[4,5,12,13].

After the introduction of the first antipsychiatric drug, chlorpromazine, which rendered excellent results, along with increasing public concerns of risks and side effects from frontal lobotomy, led to nearly extinction of psychosurgery. Only few centers still performed the procedures until now[4,5].

Modern psychosurgery

Because Freeman's technique was very crude and non-selective, other neurosurgeons at that time tried to develop more selective procedures.Scoville was the first person who reported selective cortical undercutting procedure, reflected attempt to localize the lesioning area[4,5].

After the stereotactic surgical system was developed in the late 19th century, it was improved to the level that virtually any area of the brain can be access in minimally invasive way[14]. In 1949, Spiegel and Wycis performed the first stereotactic dorsomedial thalamotomy for treatment of mental disorders. In the same year, Leksell, a Swedish neurosurgeon, developed a more practical stereotactic system. He and Talairach, a French neurosurgeon, developed anterior capsulotomy procedure for treatment of refractory psychiatric illness which still use nowadays. Other stereotactic systems such as Cosman-Roberts-Wells (CRW) system were also developed. These led to minimal-invasive way of psychosurgery with markedly reduced morbidity and mortality and truly revolutionized psychosurgery into modern era[4,5,13,15].

Besides stereotactic ablative surgery, radiosurgery was used for clinical treatment since 1958 by Leksell. Main procedures were anterior capsulotomy for psychiatric illnesses and other functional neurosurgery. Radiosurgery was considered truly noninvasive ablative procedure and still being used for treatment of psychiatric diseases[4,5,16].

Rise of neuromodulation

Neuromodulation for treatment of psychiatric illness was first performed by Robert Health, a psychiatrist, in 1950s. He used cerebellar vermis as a target for stimulation but it had little success[4,5].

After 1970s, concepts of deep brain stimulation (DBS) were used for treatment of movement disorders with good response. This led to approve of DBS for treatment of essential tremor by FDA in 1987 and then other movement disorders[17]. Concepts of DBS was soon introduced for treatment of psychiatric diseases. Results from trials found DBS to be effective for treatment of obsessive compulsive disorder (OCD), affective disorders and other indications, such as drug addiction, anorexia nervosa. DBS for psychosurgery is now one of the most rapid evolving field in neurosurgery[4,5,15,18].

On the other hand, concepts of peripheral stimulation were also developed. Vagus nerve was founded to have effects on brain due to its large brain projection.Vagus nerve stimulation (VNS) was successfully used for treatment of intractable epilepsy. Evidences suggested that VNS also improved mood of epilepsy patients, this led to trials of VNS for mood disorders later[4,5,19].

Physiology of psychosurgery

Unlike movement disorders, mechanisms underlying psychiatric diseases are unclear. Most importantly due to the lack of reproducible animal models, such as MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) model in Parkinson's disease[17,20]. Knowledge of psychiatric diseases comes from case studies, experiences in previous treatment and recently, functional imagings[4,5,18,20].

The limbic system was first described by Papez who proposed the reverberating brain circuit responsible for memory and emotion[21,22]. The system consists of cortical, subcortical and diencephalic structures. It has a crucial role in emotion,memory, learning and motivation. Malfunction of the limbic system is thought to be cause of psychiatric illness so that the term "psychosurgery" should be called "limbic system surgery"[4,5,20].

Although less well-defined, various evidences suggest that major mechanisms of psychiatric illness is malfunction of neuronal circuits. The cortico-striato-thalamic circuits are considered to have central role for pathophysiology of the diseases and also for considering the treatments, such as brain targets for lesioning or neuromodulation[18,20,23]. In OCD, multicircuits link between the orbitofrontal cortex, prefrontal cortex, striatum, thalamus and cingulate cortex are postulated. Symptoms of OCD occur when there is an imbalance of activity between these circuits[18,20,23]. In major depressive disorder (MDD) the patho-physiology is more complex and heterogenous. Symptoms are considered to be from failure of system to response with stress, not a single circuit or specific brain region. This system has many components in cortical, subcortical and limbic system[18,20].

Patient selection

Patients should be diagnosed according to the DSM IV criteria. OCD and MDD are major indications for psychosurgery. Other diseases are Tourette syndrome, drug addiction, chronic pain (especially if it has depressive mood component), severe aggression and self-mutilation[4,5]. Patient should be clinically severe, chronic, disabling and refractory to conventional treatment[18,24,25]. Treatment failure should include drugs (which must be adequate in terms of dosage, duration and adherence), psychotherapy and in some cases, electroconvulsive therapy (ECT). Severity should be assessed by validate clinical research scale. This is helpful for patient selection and also for evaluation of treatment responsiveness. Generally, Yale-Brown Obsessive Scale (Y-BOCS) is used for OCD which about 30% reduction of score is considered to be effective. For major depression, the Hamilton Rating Scale (HDRS), Montgomery-Asberg Depression Rating Scale (MADRS) or Beck Depression Inventory (BDI) score are commonly used. These scales are quantitative assessment and important for comparison of the results[18,24,25].

Ideally, psychosurgery should be conducted in the center that has multidisciplinary team, such as neurosurgeon, neurologist and psychiatrist. Medical records should be carefully reviewed. Investigations, such as neuroimagings, EEG should be performed as need. All members of the team should agree to perform psychosurgery[24,25].

The family support is also crucial. They must be informed about evaluating process, indications, risks and benefits of the surgery. They must be clearly understand that psychosurgery is only a part of treatments and agree to further support the patient in a long-term[24,25].

Ablative procedure

Anterior cingulotomy

After functions of the cingulate cortex were studied extensively by Fulton and other neuroanatomists, he suggested that the anterior cingulate cortex could be target for psychiatric illnesses. Electrophysiologic studies in human and clinical cases also supported this idea[13,20,23,26].

The cingulate gyrus locates along the corpus callosum, at medial part of the cerebral hemisphere. It consists of the mesocortex which has 3 to 5 layers. The cingulate cortex can be divided into anterior and posterior part. The anterior cingulate cortex has executive functions and can be further subdivided into cognitive dorsal and affective ventral portion. The posterior cingulate cortex is a part of limbic system. White matter core of the cingulate cortex is called the cingulum. The cingulate cortex has extensive connections to various parts of the brain[20,23,26].

Initially, cingulotomy was performed by open technique, cingulectomy, but it has considerable complications[26]. Later, stereotactic cingulotomy was described by Foltz and White for intractable pain with good results if patients had affective components. Ballantine first introduced stereotactic cingulotomy to USA in 1967[4,5,26,27]. It became the most commonly performed modern psychosurgery in North America nowadays. Common indications are refractory OCD, treatment refractory depression (TRD) and, to a lesser

degree, also for drug addiction, severe aggression and intractable pain[25-27]. Results of stereotactic cingulotomy are difficult to compare among studies due to highly heterogeneity in terms of patient selection criteria, operative techniques, surgical target, result measurement or follow-up period. Generally, cingulotomy for intractable OCD and MDD has success rate about 30 to 50%[25-33]. A large case series of 198 patients suffering from various psychiatric illnesses reported by Ballantine, showed 62% worthwhile improvement in patients with severe affective disorder and 56% in OCD with very low complication rates[27]. Complications included urinary retention, dizziness, seizure. These were usually mild and self-limited[25-27].

For pain treatment, patients should have medical refractory pain with significant psychiatric component, such as cancer pain. Various studies showed good pain relief in 30 to 80% of patients after cingulotomy[34-36].

Surgical target for cingulotomy is now usually base on CT or MRI-guided stereotactic imaging. Targets are set at the bilateral cingulated gyrus (Fig. 1), 2 to 2.5 cm posterior to tip of frontal horn of the lateral ventricle, 7 mm from the midline, and 2 to 3 mm above the corpus callosum. Using thermocoagulation electrode, 2 lesions are made 5 mm apart along the electrode axis[27]. In severe cases, 3 consecutive lesions may be made along cingulated gyrus. Lesioning also be repeated later or combined with other ablative techniques[37,38]. However, there is no randomized control trial or standardization for lesioning techniques.

Subcaudate tractotomy

Geoffrey Knight, a British neurosurgeon, first performed subcaudate tractotomy in 1964. Initially, he used radioisotope then radiofrequency ablation. Target for subcaudate tractotomy was about area of substantia inominata below head of the caudate (Fig. 2). This procedure aims to disconnect area of basal frontal lobe. Target was at 15 mm from the midline, 10 mm above level of the planum sphenoidale, at the most anterior part of the sella turcica[39,40].

A large series of subcaudate tractotomy by Knight, performed in 249 patients with severe mood disorder or OCD founded that 34% of patients had improvement at 1 year after the surgery. Other case series also reported improvement rate in approximately 30 to 100%[30-32,39-41].

Limbic leucotomy

Limbic leucotomy is a combination of anterior cingulotomy and subcaudate tractotomy (Fig. 3), which aims to more complete disruption of limbic circuits. It was first introduced by Kelly and Richardson in 1970s[4,5]. Limbic leucotomy can be performed in a single-multilesion procedure or multistage procedure, such as cingulotomy followed by subcaudate tractotomy if not respond, depending on severity of symptoms[37,38,42]. Limbic leucotomy was used for treatment of refractory OCD or MDD with response rate about 30 to 50%. There was no randomized control trial between limbic leucotomy and its single component. For available evidences, results were not

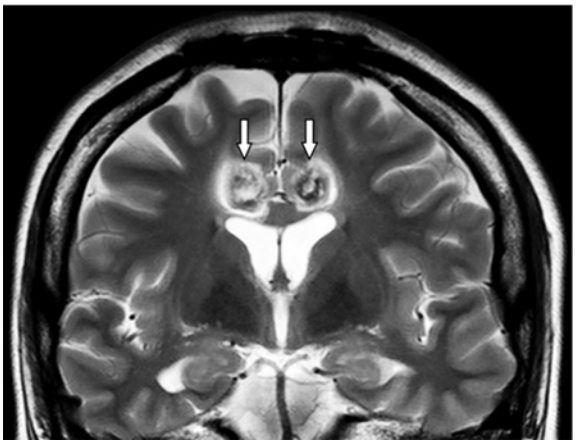

Fig. 1 Coronal MRI of the brain after anterior cingulotomy showing lesions at the anterior cingulate gyri (arrows).

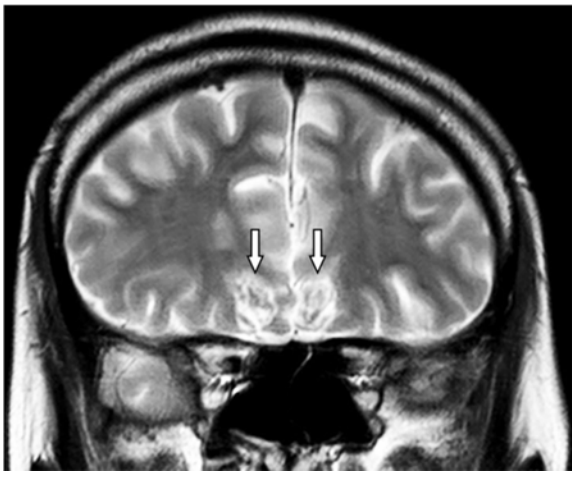

Fig. 2 Coronal MRI of the brain following subcaudate tractotomy showing lesions at the substantia innominata (arrows).

different[30-32,37,38,42].

Anterior capsulotomy

This procedure was first introduced by Talairach and Leksell for treatment of various psychiatric diseases. Anterior capsulotomy is still widely used in Europe[4,5,43]. The procedure was aimed to disconnect cortico-thalamic connections at the anterior limb of internal capsule[20,43-45]. The target described by Leksell was at the anterior limb of internal capsule, 5 mm behind the tip of frontal horn, 20 mm lateral to the midline at the level of the intercommisural plane. Lesioning could be done by thermocoagulation or radiosurgery (Fig. 4). This target also evolved to the term ventral capsule/ventral striatum (VC/VS) target for DBS leads implantation[43-45].

Common indications for anterior capsulotomy are refractory OCD and MDD with overall response rate about 50%[29-33,43,44]. The most common complications from anterior capsulotomy is weight gain which occurs in a large number of patients[29,32,33,43,44].

Amygdalotomy

In animals, temporal lobe resection was long ago found to reduce aggression. Later, the amygdala nucleus was found to be a component of the limbic system and responsible for aggressive behavior. Narabayashi et al firstly reported a series of bilateral stereotactic amygdalotomy in 60 patients in 1963[46]. Since their report, there had been other reports of stereotactic amygdalotomy with various results. Improvement rates ranged from 33 to 100%. Complication rates ranged from 0 to 42%, including death. These might be due to mark heterogeneity between studies. Patient selections varied between studies, which some included epilepsy patients. Stereotactic techniques, lesioning methods and exact parts of the amygdala were also different[46-49].

Due to improvement of psychiatric drugs and uncertain result of amygdalotomy, very few amygdalotomy was performed nowadays. However, there still is need for amygdalotomy in some patients with failure of conventional treatments of aggression[46-49] (Fig. 5).

Neuromodulations

Deep brain stimulation

After introduction of DBS in 1990s, it became established as a surgical treatment for movement disorders, such as Parkinson's disease, tremor and dystonia[17]. DBS was first used for OCD in 1999 by

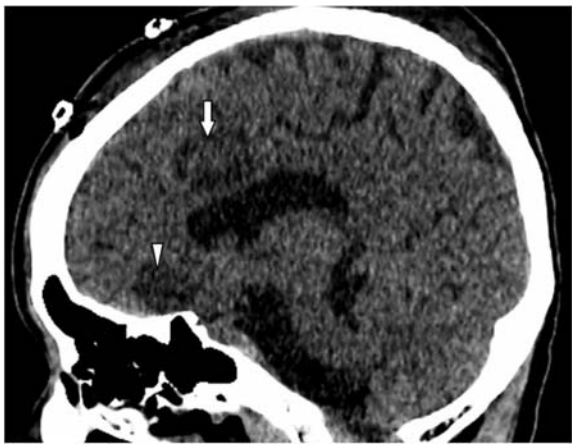

Fig. 3 Sagittal CT of the brain after limbic leucotomy showing combined lesions of anterior cingulotomy (arrow) and subcaudate tractotomy (arrowhead).

Fig. 4 Axial CT of the brain after anterior capsulotomy showing lesions at the anterior limbs of internal capsule (arrows).

Nuttin et al[4,5]. DBS was then rapidly adopt to psychosurgery and became one of the most rapid evolving field in neurosurgery. The acceptance was from perception of DBS as a non-destructive type of surgery and also adjustable parameters. Importantly, evidences showed that it was safe to perform bilaterally[17,18,50].

Refractory OCD and MDD are common indications for DBS. Other indications include Tourette

syndrome, drug addiction, anorexia nervosa and likely to expand in the near future[4,5,18,32,44,45,50-57]. For OCD, the most common described target in the literatures is VC/VS and this led to FDA approval of VC/VS DBS for OCD treatment in 2009. However, the optimal target for OCD is still not known. Other targets for OCD are the nucleus accumbens, bed nucleus of stria terminalis, subthalamic nucleus, inferior thalamic peduncle and globus pallidus internus. For MDD, common targets are VC/VS and subgenual cingulate (Cg25). Indications and targets of DBS for psychiatric disorders are summarized in Table 1.

Fig. 5 Axial CT of the brain following amygdalotomy showing lesions at the amygdalas (arrows).

Despite its attractiveness, efficacy of DBS for psychiatric illnesses was not superior when compared with that of ablative procedures. Moreover, complications of DBS might be higher. DBS is a high cost, hardware-based surgery that prone to infection, need regular visits and careful parameter adjustments. It should be considered as an investigational therapy compared with ablative procedures, which have been more established[18,24,32,44,50].

Vagus nerve stimulation

After used in epilepsy patients and founded to improve mood of the patients, VNS was later used in pure mood disorders[58]. VNS was used for refractory depression. Although mechanism is unclear, VNS can be benefit in about 30% of patients with depression. Long-term effect of VNS may be more pronounced than in a short-term[32,33,58-60]. In 2005, FDA approved VNS as an adjunctive therapy to medication for treatment of depressive episodes that failed to medical therapy. Systematic review confirmed the efficacy of VNS, but randomized control trial is still needed[59].

Siriraj's experiences in psychosurgery

Since 2013, 8 cases of psychiatric patients underwent psychosurgery. Unlike the literatures, the

Table 1. Indicationsand targets of DBS for psychiatric disorders

Psychiatric disorder	DBS target
Obsessive compulsive disorder[18,44,45,50-52]	Anterior limb of internal capsule
	Nucleus accumbens
	Ventral capsule/ventral striatum (VC/VS)
	Subthalamic nucleus
	Inferior thalamic peduncle
Major depressive disorder[18,32,50,51,53,54]	Subcallosal cingulate gyrus (Brodmann area 25)
	Ventral capsule/ventral striatum (VC/VS)
	Interior thalamic peduncle
	Nucleus accumbens and anterior limb of internal capsule
	Stria medullaris thalami (habenula)
Anorexia nervosa[18,50,51,57]	Subcallosal cingulate gyrus (Brodmann area 25)
	Nucleus accumbens
Drug addiction[18,50,51]	Nucleus accumbens
Tourette syndrome[18,50,55,56]	Thalamus (centromedian parafascicular complex)
	Globus pallidus internus (Gpi)
	Ventral capsule/ventral striatum (VC/VS)

most common indication of our psychosurgery is intractable aggression in 4 patients. Other indications included self-mutilation disorder, intractable pain with depressive mood, delusional disorder and paranoid schizophrenia with intractable aggressive behavior. This might be stem from notorious history of psychosurgery that makes psychiatrists reluctant to refer intractable cases to neurosurgeon for psychosurgery unless there is heavy burden to treating physicians or family members. All patients were undergone ablative procedures due to low cost and good efficacy. These procedures consisted of anterior cingulotomy, amygdalotomy, limbic leucotomy and anterior capsulotomy. Most patient undergone a single operation, but 3 patients required multiple operations. This may indicated complexity of disease's circuits. The overall results were good. Aggressiveness was markedly decreased and patient care was a lot easier postoperatively. After this successful pilot case series, we expect psychosurgery becoming an important alternative for the treatment of intractable psychiatric disorders in the future.

Conclusion

Psychosurgery has a long and interesting history. Since its origin, psychosurgery had been through a tough road. From rising to falling, almost extinct, now psychosurgery revives again. Advances in surgical techniques and insights for pathophysiology of the diseases make modern psychosurgery a lot more effective and safe. Both types of psychosurgery, ablation and neuromodulation, are performed nowadays. Each has its own advantages and disadvantages. Results of psychosurgery are promising and there is still a room for improvement. In the near future, this rapid evolving field might become important treatment for intractable, deliberating psychiatric patients.

What is already known from this topic?

Psychosurgery has a long history across the century. It still plays a major role for the treatment of intractable psychiatric illness. Neurosurgical methods, including stereotactic ablation and DBS on various targets in the brain, and VNS render favorable outcomes with minimal adverse effects in well selected cases.

What this study adds?

Ablative stereotactic neurosurgery, including anterior cingulotomy, subcaudatetractotomy, limbic leucotomy and amygdalotomy, is effective for controlling severe treatment-resistant psychiatric symptoms. Anterior cingulotomy, amygdalotomy and limbic leucotomy can suppress aggressive behavior. Limbic leucotomy can be used for controlling self-mutilation and OCD symptoms. However, psychosurgery is underutilized in the present owing to its infamous use in the past and lack of experience in patient selection. This therapeutic option should be considered in patients with refractory psychiatric disorders.

Potential conflicts of interest

None.

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การนำการผ่าตัดรักษาโรคทางจิตเวชมาใช้อีกครั้ง: การผ่าตัดทางประสาทศัลยศาสตร์ในปัจจุบันสำหรับโรคทางจิตเวช

โชติวัฒน์ ตันศิริสิทธิกุล, บรรพต สิทธินามสุวรรณ

ภูมิหลัง: ผู้ป่วยทางจิตเวชจำนวนหนึ่งไม่ตอบสนองต่อการรักษามาตรฐานอันประกอบด้วย ยา จิตบำบัด และการรักษาด้วยไฟฟ้า การผ่าตัดเพื่อรักษาโรคทางจิตเวชนับเป็นทางเลือกในการรักษาผู้ป่วยดังกล่าว ประวัติศาสตร์ของการผ่าตัด โรคทางจิตเวชมีความน่าสนใจและยังมีผลต่อการตัดสินใจรักษาในปัจจุบันด้วย

วัตถุประสงค์: การผ่าตัดเพื่อรักษาโรคทางจิตเวชมีเป้าหมายเพื่อลดอาการที่รุนแรงของโรคและมีผลข้างเคียงน้อยที่สุด

วัสดุและวิธีการ: คณะผู้นิพนธ์ทบทวนบทความและงานวิจัยทางการแพทย์เกี่ยวกับประวัติศาสตร์, วิธีการผ่าตัด และผลลัพธ์ของการผ่าตัดรักษาโรคทางจิตเวช

ผลการศึกษา: การผ่าตัดรักษาโรคทางจิตเวชนั้นเกือบจะสูญหายไปเนื่องจากการพัฒนายาทางจิตเวชที่ดีขึ้น เทคนิคการผ่าตัดที่หยาบและการคัดเลือกผู้ป่วยสำหรับผ่าตัดที่ไม่ดี อย่างไรก็ตามมีผู้ป่วยจิตเวชจำนวนหนึ่งไม่ตอบสนองต่อการรักษามาตรฐานอันประกอบด้วยยา จิตบำบัด และการรักษาด้วยไฟฟ้า การผ่าตัดรักษาโรค ทางจิตเวชนับเป็นทางเลือกเพื่อบรรเทาอาการในผู้ป่วยเหล่านี้ ปัจจุบันการผ่าตัดรักษาโรคทางจิตเวชได้รับความสนใจขึ้นมาอีกครั้งเนื่องจากเทคนิคการผ่าตัดมีความแม่นยำและปลอดภัยมากขึ้นความเข้าใจพยาธิสรีรวิทยาของโรคที่ดีขึ้น รวมไปถึงการพัฒนาการผ่าตัดเพื่อฝังขั้วไฟฟ้าโดยไม่ทำลายเนื้อสมอง สิ่งเหล่านี้ทำให้การผ่าตัดรักษาโรคทางจิตเวช มีความก้าวหน้าและเป็นที่แพร่หลายมากขึ้นในอนาคต

สรุป: ในบทความกล่าวถึงประวัติศาสตร์ของการผ่าตัดรักษาโรคทางจิตเวชความรู้พื้นฐานเกี่ยวกับพยาธิสรีรวิทยาของโรคแนวทางการคัดเลือกผู้ป่วยสำหรับผ่าตัด การผ่าตัดแต่ละวิธีรวมทั้งผลลัพธ์ของการผ่าตัด