



Psychosurgery role in Depressive Disorders

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Major depressive disorder (MDD)

Epidemiology

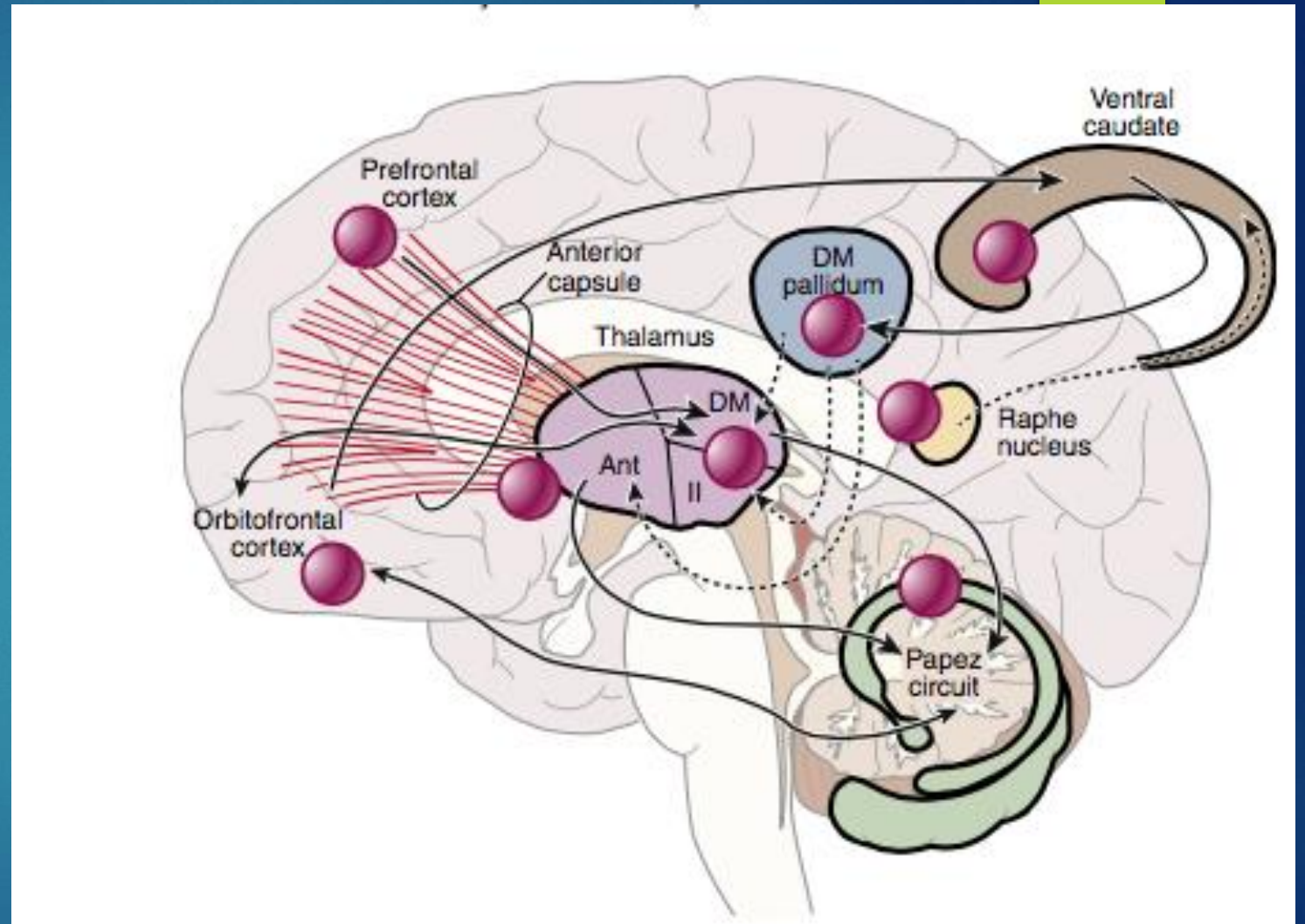
- ▶ MDD is one of the most disabling and common diagnoses throughout psychiatric disorders.
- ▶ **12%** of men and **20%** of women will experience a major depressive episode (MDE) in their lifetime.
- ▶ The mainstay of MDD treatment is a combination of psychotherapy and pharmacotherapy .

treatment-resistant depression (TRD)

- ▶ up to **30%– 40%** of patients remain depressed despite optimal care, and are characterized as having treatment-resistant depression (TRD) .
- ▶ significantly impaired, unable to work, poor personal relationships and quality of life.
- ▶ 1 Up to 15% of TRD patients commit suicide.

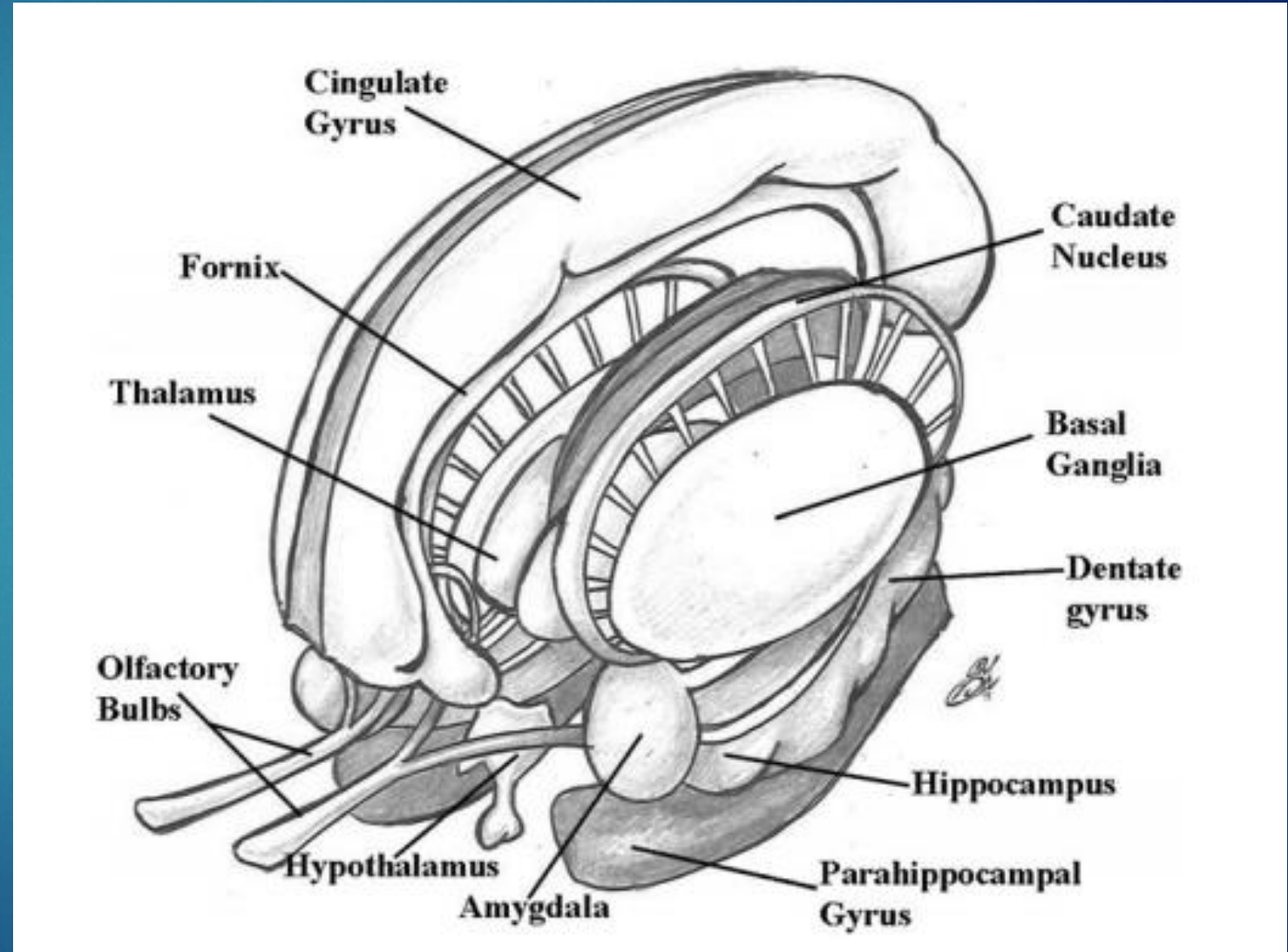
what results in Depression?

- ▶ any **dysfunction of networks** rather than an isolated structural or neurotransmitter abnormality.
- Dysfunctional activity within the **limbic frontal-striatal- thalamic- frontal loops**



Anatomical correlations of Depression

- ▶ **the Papez circuit :**
- ▶ the hippocampus,
- ▶ the fornix,
- ▶ the mammillary bodies,
- ▶ the mammillothalamic tract,
- ▶ the anterior thalamic,
- ▶ the subgenual cingulate (SCG) [Brodman area 25 or Cg25],
- ▶ the parahippocampal gyrus,
- ▶ the entorhinal cortex
- ▶ **the amygdala**
- ▶ **the hypothalamus**
- ▶ **the nucleus accumbens (NAcc)**
- ▶ **the orbitofrontal cortex**



neuro- modulation approaches may be an option for TRD patients.

- ▶ noninvasive approaches (electroconvulsive therapy and transcranial magnetic stimulation)
- ▶ invasive surgical approaches (such as lesional and stimulation-based operations)

Psychosurgery

▶ **Ablative neurosurgery :**

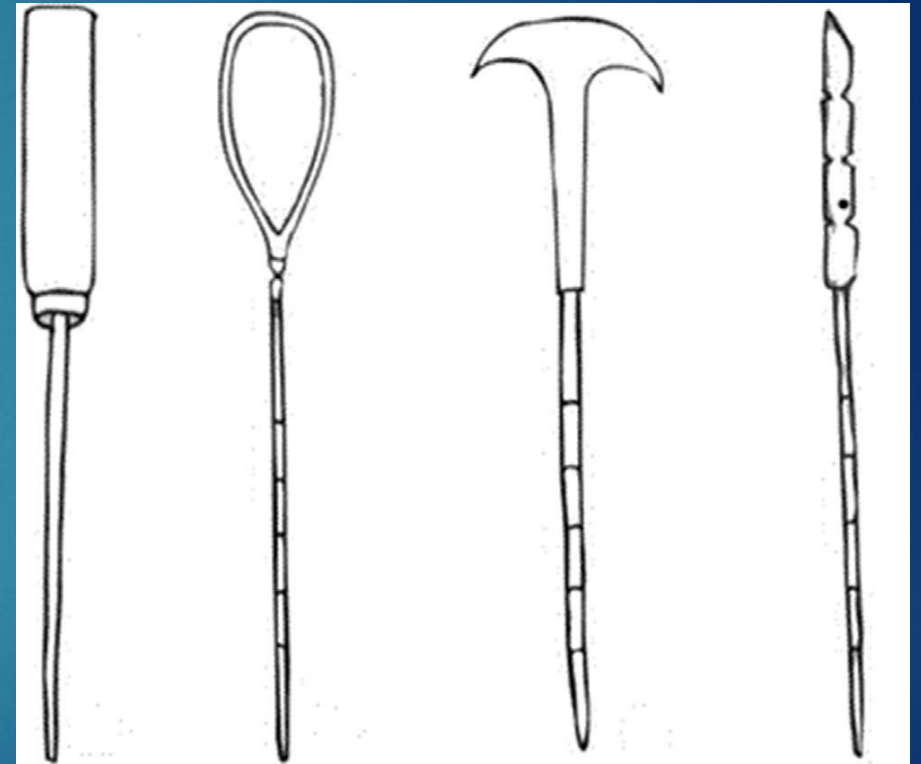
- ▶ Anterior cingulotomy
- ▶ Subcaudate tractotomy
- ▶ Limbic leucotomy
- ▶ Anterior capsulotomy

▶ **Deep brain stimulation (DBS) :**

- ▶ continues to evolve
- ▶ subcallosal cingulate cortex (SCC)
- ▶ ventral capsule/ventral striatum
- ▶ medial forebrain bundle (MFB)

A brief history OF FUNCTIONAL NEUROSURGERY: PSYCHOSURGERY

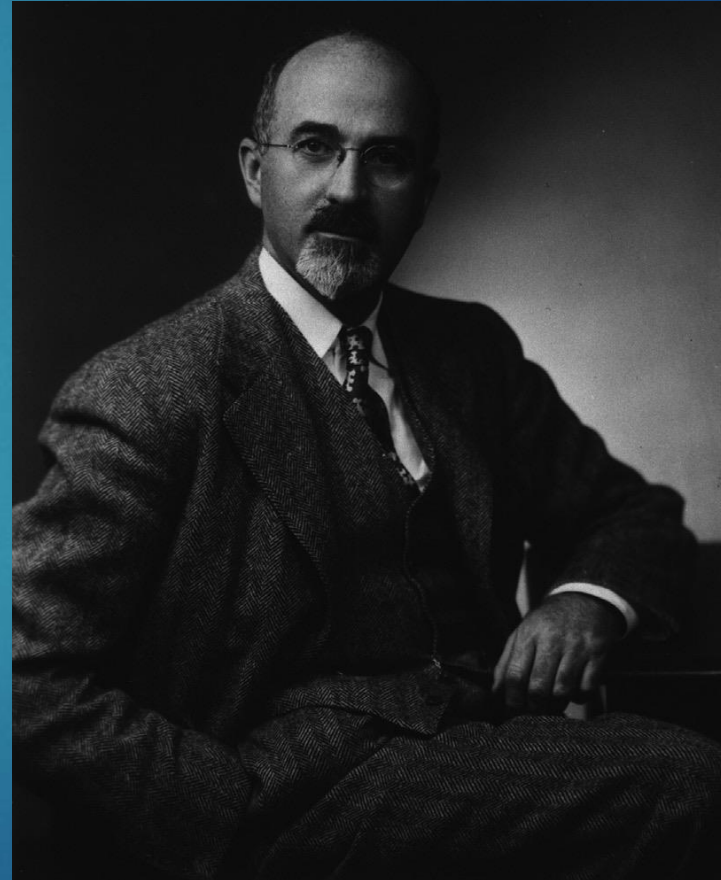
- ▶ In the late **19th** century, the correlation of neurological functions to neuroanatomy began to emerge.
- ▶ Moniz and Lima creating frontal lobe white matter lesions
- ▶ at first alcohol then leucotome was used for ablation.
- ▶ In 1949, Moniz was awarded the Nobel Prize for the **Leucotomy** procedure.




Freeman (neuropsychiatrist) and James
Watts (neurosurgeon)

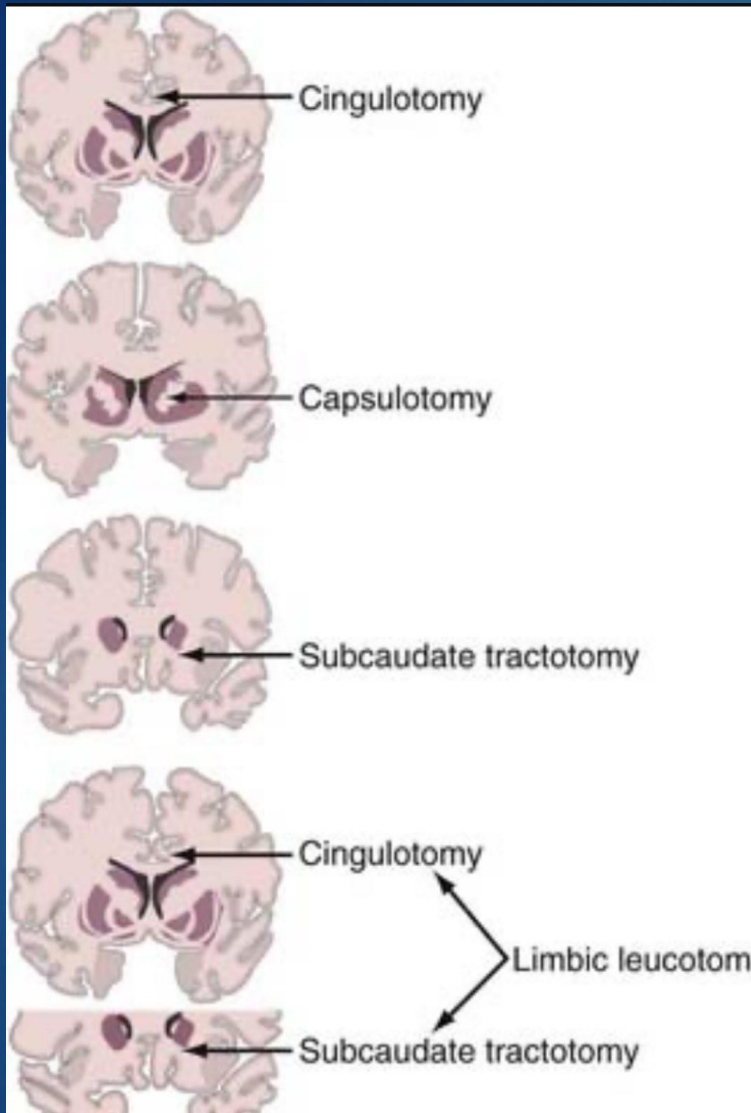
Transorbital leucotomy (also
known as the “icepick” procedure) was
developed by Freeman in 1948

Some of the first *prefrontal lobotomies*
frontal lobe syndrome.
post-leukotomy syndrome



Freeman

- 
- ▶ In **1949**, Scoville described three frontal **undercutting** techniques.
 - ▶ Mettler then introduced the **frontal topectomy**, a gray matter ablative procedure of BA 9, BA 10, and BA 46.
 - ▶ Spiegel and Wycis introduced the **mesencephalothalamotomy** in order to treat intractable pain.
 - ▶ refinement of stereotactic methodology



As a result, four ablative procedures were developed to treat depression:

- anterior cingulotomy,
- Sub-caudate tractotomy
- limbic leucotomy,
- anterior capsulotomy.

Nucleus Accumbens (Nacc)

- reward processing
- anhedonia
- the emotional memory associated with depression

Subcallosal Cingulate Cortex

- The SCC (a.k.a. Cg25; Brodmann area [BA] 25)
- decision making and emotional processing basal vegetative functions, and autonomic states.

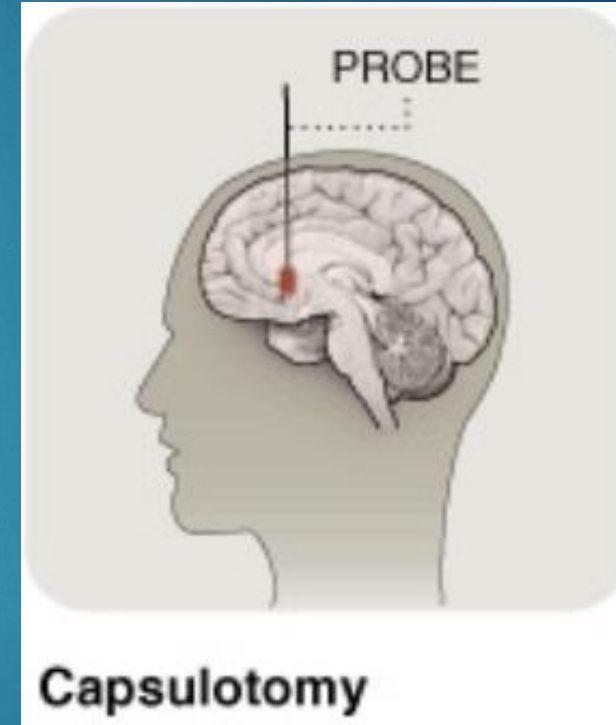
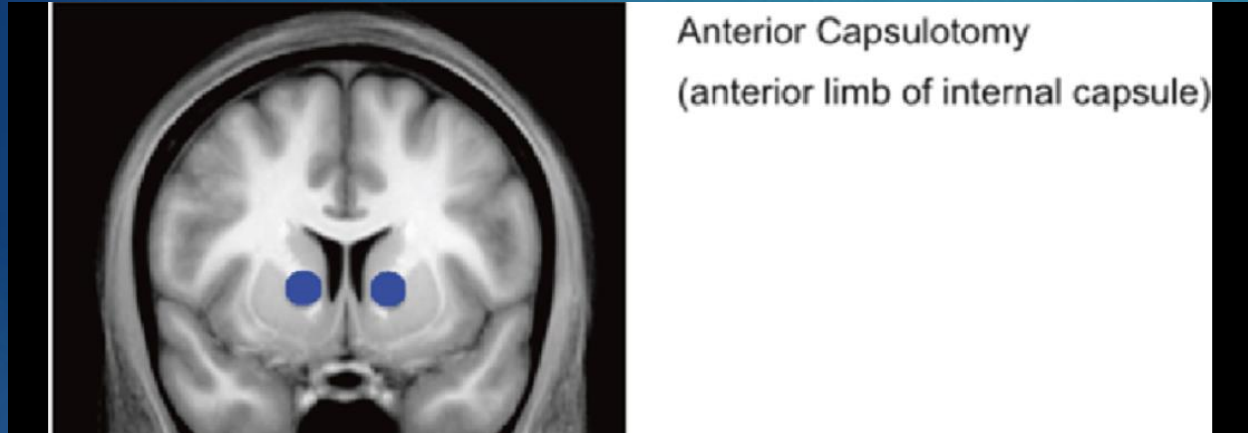
Anterior Limb of the Internal Capsule (ALIC)

- humans, rodents, and other animals
- higher cognitive processing of reward information

Medial Forebrain Bundle (MFB)

- emotional decision making

the anterior limb of the internal capsule (bilateral anterior capsulotomy – **BAC**),

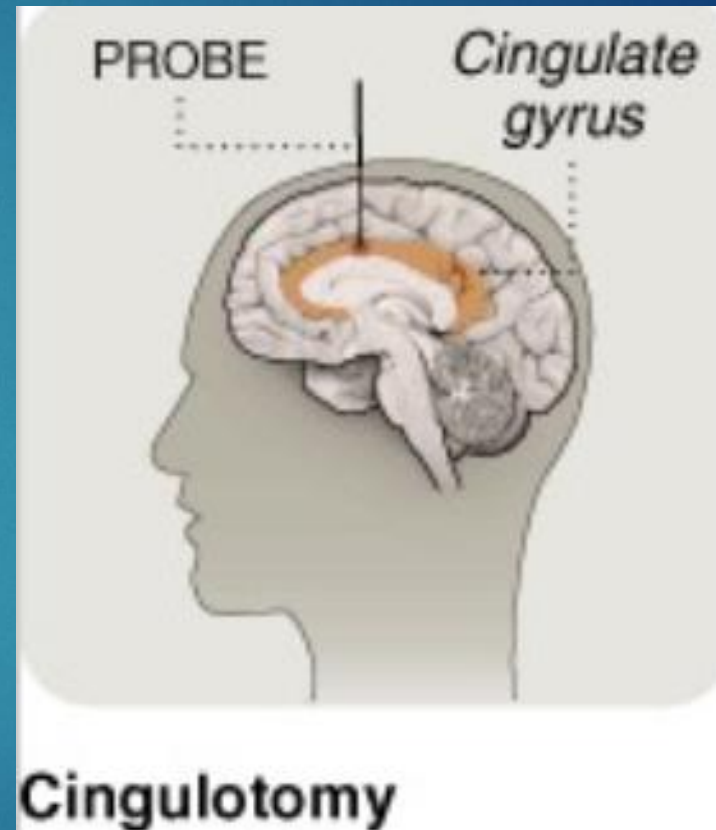


the supragenual anterior cingulate gyrus and cingulum (bilateral anterior cingulotomy –

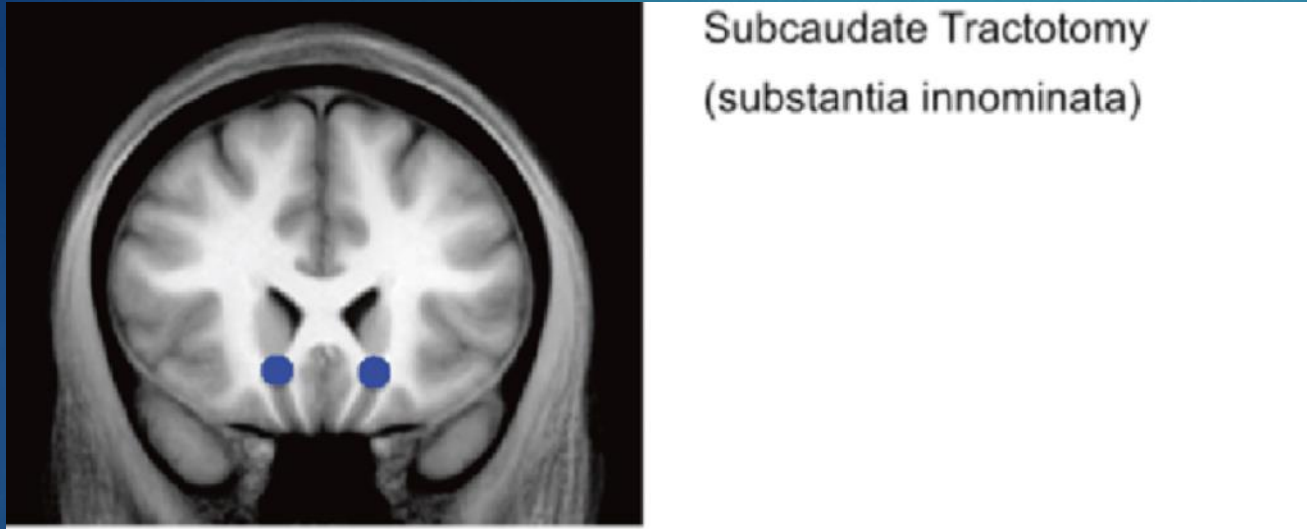
BACING)



Anterior Cingulotomy
(anterior cingulate gyrus)

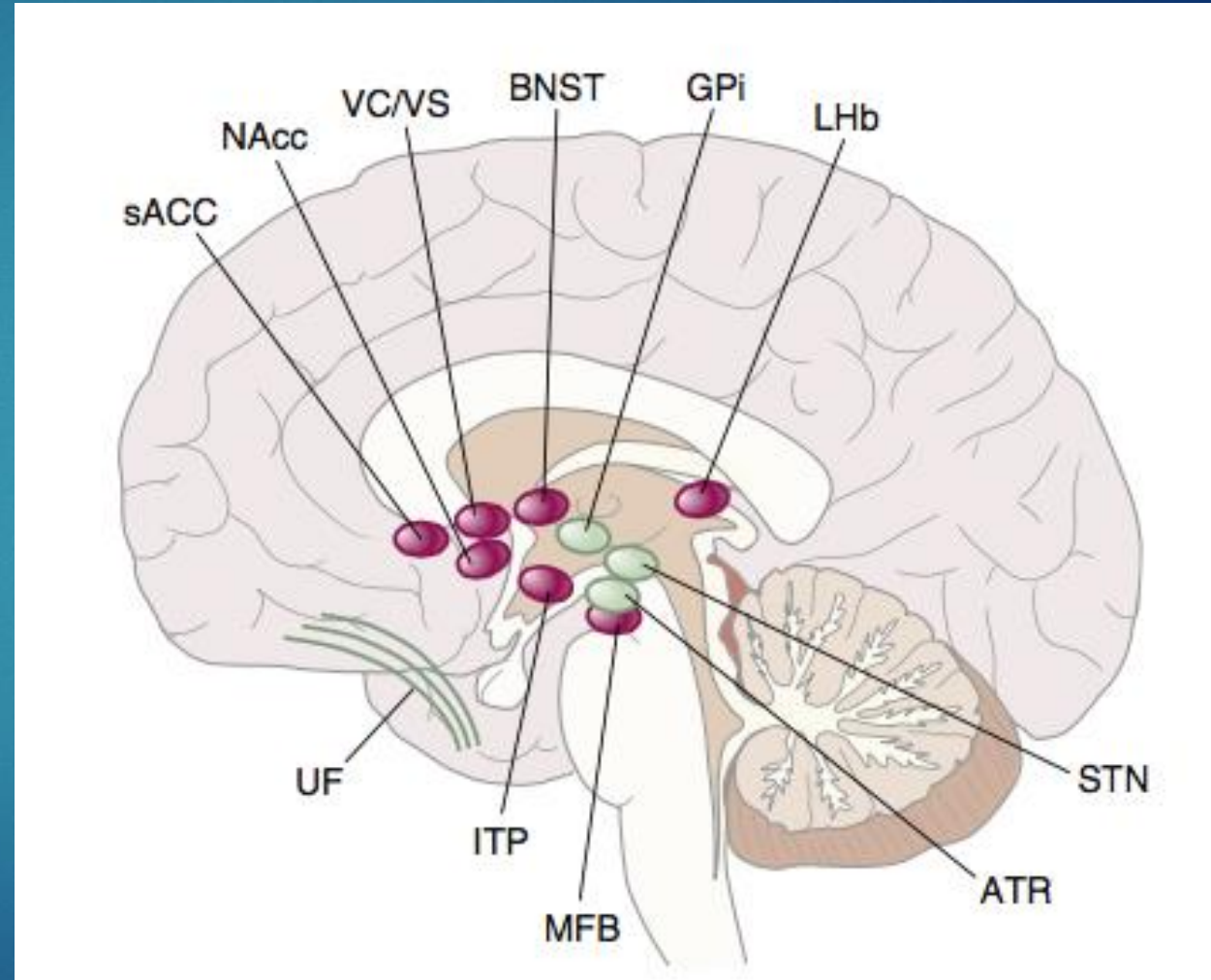


Sub-genial anterior cingulate gyrus and subcortical orbitofrontal white matter (bilateral sub-caudate tractotomy – **BST**)



A combination of BACING and BST is known as limbic leukotomy (bilateral limbic leukotomy – **BLL**)

- **Nucleus Accumbens (NAcc)**
- **Subcallosal Cingulate Cortex**
- **Anterior Limb of the Internal Capsule (ALIC)**
- **Medial Forebrain Bundle (MFB)**



DEEP BRAIN STIMULATION

- ▶ DBS is by definition a **circuit-selective** intervention likely acting on **circuit-specific symptom** profiles.
- ▶ DBS is currently approved for the management of Parkinson disease, dystonia, and essential tremor/
- ▶ There is a preliminary evidence of the efficacy and safety of DBS for TRD in specific targets.
- ▶ May be promising in other disorders of neural circuitry such as OCD and MDD .

several targets have been proposed for DBS in MDD including

- the SCC
- Nacc
- ventral striatum/ventral capsule (VC/VS)
- inferior thalamic peduncle (ITP)
- habenula,
- MFB

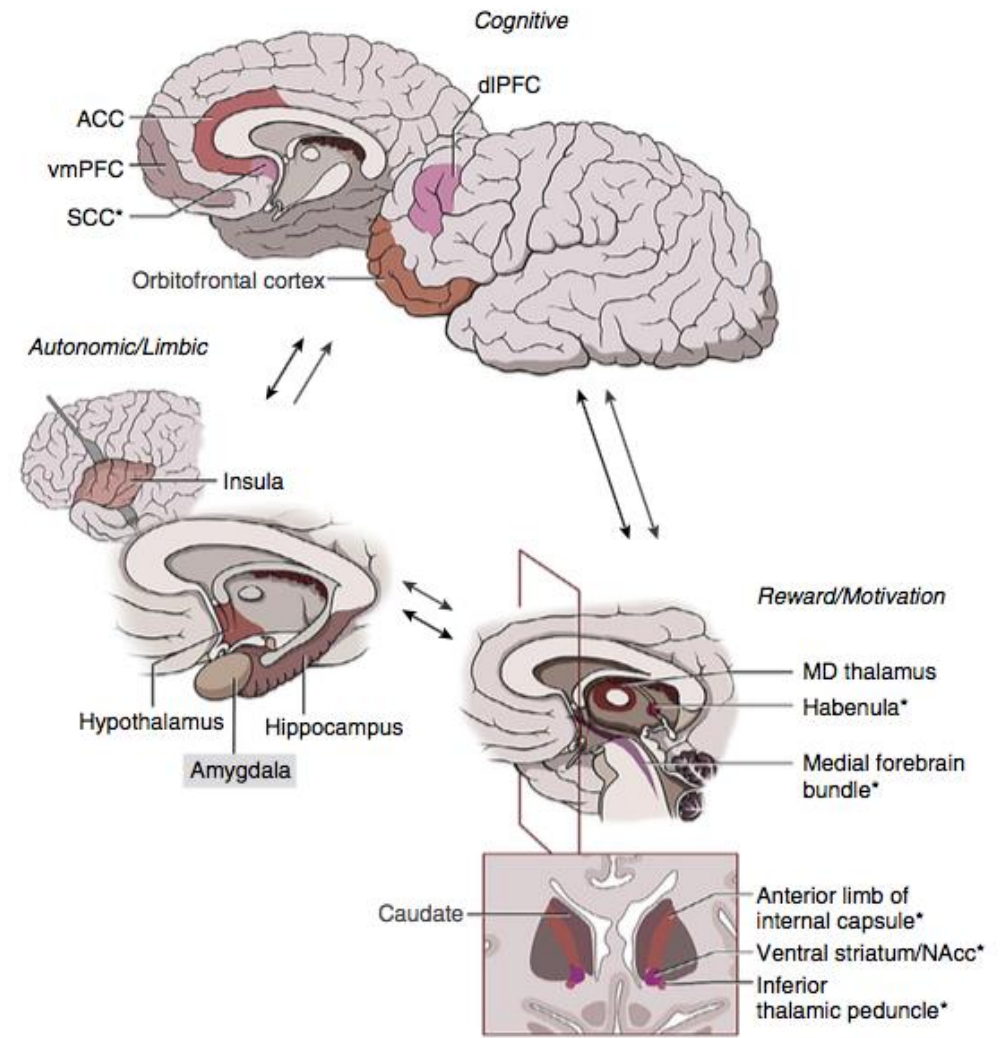


Figure 123.1. Circuit diagram for mood and anxiety disorders and deep brain stimulation targets. Deep brain stimulation at areas with an asterisk are in current use or evaluation. ACC, Anterior cingulate cortex; dlPFC, dorsolateral prefrontal cortex; MD, mediodorsal; NAcc, nucleus accumbens; SCC, subcallosal cingulate cortex; vmPFC, ventromedial prefrontal cortex. (From Lozano AM, Lipsman N: Probing and regulating dysfunctional circuits using deep brain stimulation. *Neuron*. 2013;77:406–424.)

DBS thus remains an unproven but potentially useful and effective invasive but nondestructive neurosurgical intervention for TRD.

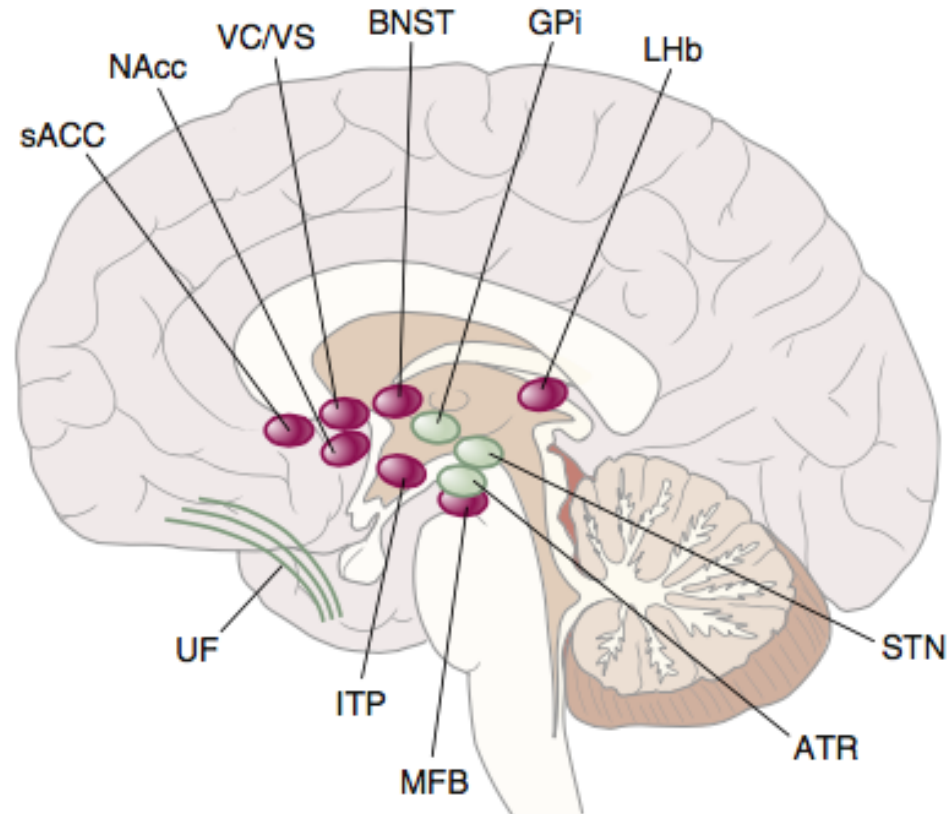
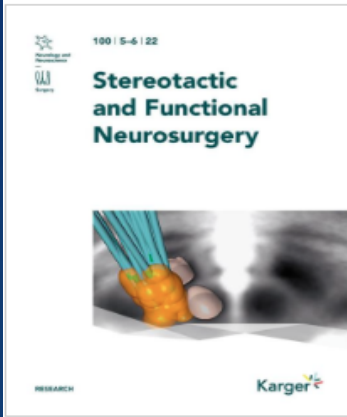


Figure 123.2. Current (red) and proposed (green) DBS targets. ATR, Anterior thalamic radiation; BNST, bed nucleus of the stria terminalis; GPI, globus pallidus interna; ITP, inferior thalamic peduncle; LHb, lateral habenula; MFB, medial forebrain bundle; NAcc, nucleus accumbens; sACC, subgenual anterior cingulate cortex; STN, subthalamic nucleus; UF, uncinate fasciculus; VC/VS, ventral capsule/ventral striatum. (Modified from Anderson RJ, Frye MA, Abulseoud OA, et al. Deep brain stimulation for treatment-resistant depression: efficacy, safety and mechanisms of action. *Neurosci Biobehav Rev.* 2012;36(8):1920–1933.)



Ablation Surgeries for Treatment-Resistant Depression: A Meta-Analysis and Systematic Review of Reported Case Series Free

Subject Area: Neurology and Neuroscience , Surgery

Trevor A. Hurwitz ; Christopher R. Honey ; Amir Ali Sepehry

Stereotact Funct Neurosurg (2022) 100 (5-6): 300–313.

<https://doi.org/10.1159/000526000> Article history

PubMed:35973404

- ▶ BST provides the best outcome (71% responder rate)
- ▶ BACING (aggregate responder rate of 44%) and BAC (aggregate responder rate of 40%) yield almost equivalent outcomes.
- ▶ BAC as a standalone NIMD appears to be the most effective and safest of the ablative procedures with a well-defined target.

Effectiveness and safety of neuroablation for severe and treatment-resistant obsessive–compulsive disorder: a systematic review and meta-analysis

Yijie Lai, Tao Wang, Chencheng Zhang, Guozhen Lin, Valerie Voon, Jinwoo Chang and Bomin Sun

J Psychiatry Neurosci September 01, 2020 45 (5) 356-369; DOI: <https://doi.org/10.1503/jpn.190079>

Most of the adverse events (88.4%) were mild and transient.

- ▶ **The top 3 adverse events were :**
- ▶ **headache (14.9%),**
- ▶ **cognitive deficits (9.1%)**
- ▶ **behaviour problems (8.1%).**
- ▶ **Severe or permanent adverse events included :**
- ▶ **personality changes (2.3%)**
- ▶ **brain edema or brain cyst (1.5%)**

DBS adverse effects

- ▶ Transient adverse effects after LHb DBS such as double or blurred vision or dizziness could be reversed by lowering or changing stimulation parameters.
- ▶ a manic episode,
- ▶ impulsive behaviors,
- ▶ suicide ideation.


DBS across different targets is associated with on average **60%** response rates in previously refractory chronically depressed patients.

response rates vary greatly between patients and between studies and often require extensive trial-and-error optimizations of stimulation parameters.



Current Perspectives

Deep Brain Stimulation for Depression

Martijn Figee¹ , Patricio Riva-Posse², Ki Sueng Choi¹,
Lucia Bederson¹, Helen S. Mayberg¹, Brian H. Kopell¹

Future goals

- ▶ the reticence toward psychosurgery, even for those patients suffering from the most debilitating forms of depression, still prevails, even though recent studies have shown significant improvement in terms of quality of life with the limitation that the number of treated cases has been small .

