(i) *Deep brain stimulation (DBS).* Several basal ganglia nuclei become inactive or dysfunctional in PD. Surgical implantation of very fine electrodes in these areas can be used to keep them functionally active, a process called deep brain stimulation (DBS). The thalamus, globus pallidus interna (Gpi), or STN are target regions for DBS [182], where the electrodes are implanted, in one or both the hemispheres (Fig. 14).

In DBS, devices containing two batteries, which generate finely tuned electrical currents for stimulating those deep brain areas, are implanted in both sides in the chest under the collar bone. The electrical pulses are generated by these batteries, which can be programmed precisely according to the specific needs of the PD patient. At 3–5 year' intervals, the implanted batteries can be checked or replaced or recharged, accordingly. The DBS can reduce many primary motor symptoms of PD, and also decrease the need for L-DOPA to reduce dyskinesias [183]. In addition, the electrodes can be programmed to be turned on or off, as needed, by using a hand-held device [184]. However, the greatest disadvantage of using DBS, is that it requires surgical implantation of the device, which can cause potential complications, including stroke or hemorrhage, risk of infection, speech, or balance problems. Moreover, DBS is not effective in "atypical" parkinsonian syndromes, such as multiple system atrophy, progressive supra-nuclear palsy, or posttraumatic parkinsonism [184]. In addition, DBS is not used to treat the early stages or for treating mild symptoms of PD, or not suitable for treating the cognitive, psychological, or any other non-motor symptoms [183].

(ii) *Pallidotomy and thalamotomy.* The parts of the brain which control our voluntary movements include the globus pallidus (GP), a part of basal ganglia which has strong connections to the striatum and the thalamus. In pallidotomy, the surgeon selectively destroys a part of the GP (Fig. 15). Therefore, the synaptic connections with thalamus or striatum are altered in a way which decreases tremor, rigidity, bradykinesia, and posture abnormalities in PD patients [185].

This surgical method can also reduce the amount of L-DOPA that the PD patient requires, which can decrease drug-induced dyskinesia and dystonia. Similarly, destruction of the thalamus, known as thalamotomy, can interrupt the connections between the basal ganglia and motor cortex, in ways that can restore neurotransmitter balance (e.g. glutamate excitation) and reduce symptoms, such as tremor [185]. Thalamotomy is used mainly for controlling tremor, and it is not very effective for bradykinesia, rigidity, or dyskinesias (Fig. 15).

Cell transplantation therapy

Transplantation of neuronal stem cells into the brains of PD patients is considered to be one of the most promising approaches for treating this disease [186].

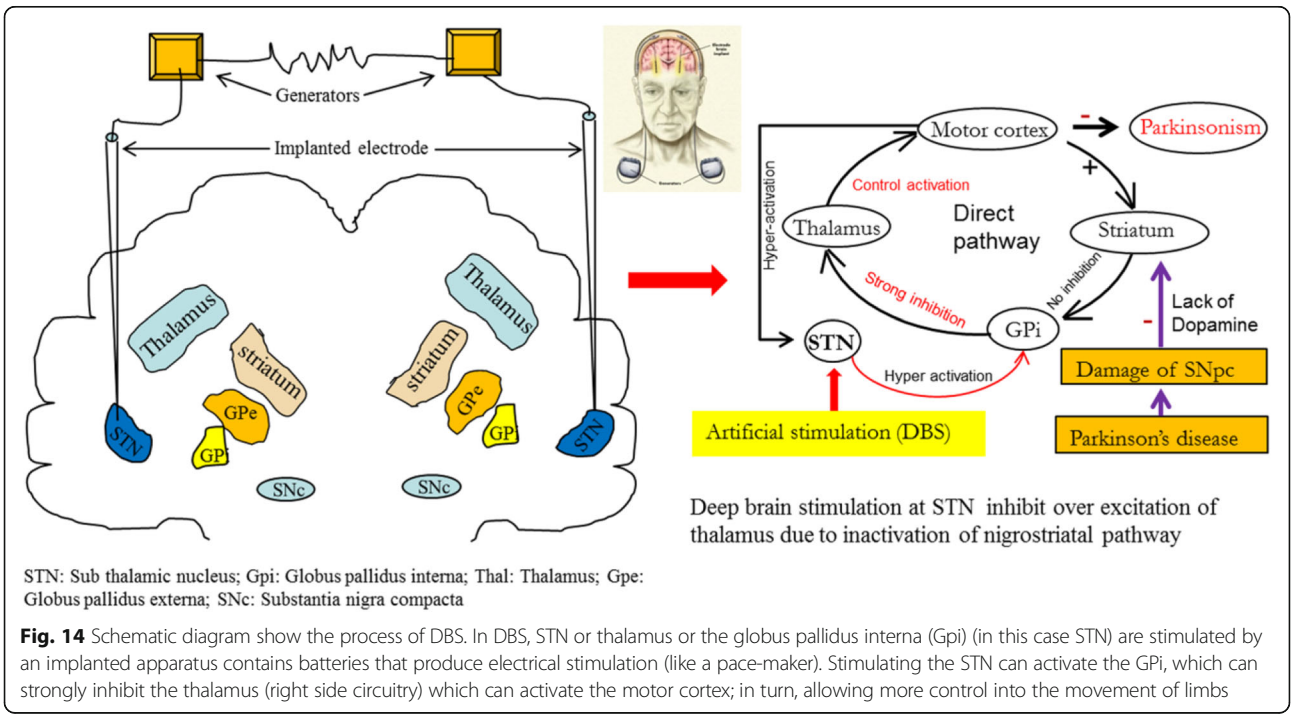

Fig. 14 Schematic diagram show the process of DBS. In DBS, STN or thalamus or the globus pallidus interna (Gpi) (in this case STN) are stimulated by an implanted apparatus contains batteries that produce electrical stimulation (like a pace-maker). Stimulating the STN can activate the GPi, which can strongly inhibit the thalamus (right side circuitry) which can activate the motor cortex; in turn, allowing more control into the movement of limbs