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## **Chronic DBS Stimulation of Minimally Conscious State: Methodological Issues**

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**Introduction:** The modulation of consciousness processes with deep brain stimulation (DBS) in minimally consciousness state seems achievable. Between 1968 and 2016 nine teams have reported effects in 58 vegetative (VS) or minimally conscious (MCS) patients. We analyzed the literature focusing on methodological issues, willing to address clinically relevant key-points for the selection of targets and design of future studies.

**Literature Review:** Half of the studies were case-reports. Most teams intended to place electrodes in the thalamus. All leads were implanted according to atlas-based coordinates. Five studies used low frequency stimulation, 25 to 50 pulses/sec, and three high frequency stimulation, at 100 and 250 pulses/sec. The most recent studies reported effects in continuing VS-MCS patients, followed up during several months or years. The clinical status and DBS effects were measured using simple clinical observations, up to JFK Coma Recovery Scale–Revised. Parallel to the clinical status, the most recent study analyzed the extent of brain lesions. No severe irreversible, stimulo-induced, adverse effects were reported, but one patient had post-operative intra cerebral hematoma. One clinical study had double-blinded on/off crossover phase, whereas the others were observational studies. From these studies it can be inferred that high or low frequency stimulation of deep gray structures, particularly of the central thalamus, can provoke overt conscious behaviors. Recent literature concerning models of consciousness related circuitry let us think that several deep brain regions and cortices are involved and could be future relevant spots of neuromodulation.

**Conclusion-Perspective:** Future studies willing to modulate the deep brain circuitry should take into account the recent knowledge on altered dynamics of neural correlates of disorder of consciousness, the dynamics of spontaneous recovery, and the consequences of structural and functional lesions.