Hypothalamic deep brain stimulation

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Due to its involvement in a wide variety of cardiovascular, metabolic, and behavioral functions, the hypothalamus constitutes a potential target for neuromodulation in a number of treatment-refractory conditions. The precise neural substrates and circuitry subserving these responses, however, are poorly characterized to date.

Neudorfer et al. sought to retrospectively explore the acute sequalae of hypothalamic region deep brain stimulation and characterize their neuroanatomical correlates. To this end they studied at multiple international centers 58 patients (mean age: 68.5 ± 7.9 years, 26 females) suffering from mild Alzheimer's disease who underwent stimulation of the fornix region between 2007 and 2019. They catalogued the diverse spectrum of acutely induced clinical responses during Electrostimulation and interrogated their neural substrates using volume of tissue activated modelling, voxel-wise mapping, and supervised machine learning techniques. In total 627 acute clinical responses to stimulation - including tachycardia, hypertension, flushing, sweating, warmth, coldness, nausea, phosphenes, and fear - were recorded and catalogued across patients using standard descriptive methods. The most common manifestations during hypothalamic region stimulation were tachycardia (30.9%) and warmth (24.6%) followed by flushing (9.1%) and hypertension (6.9%). Voxel-wise mapping identified distinct, locally separable clusters for all sequelae that could be mapped to specific hypothalamic and extrahypothalamic gray- and white-matter structures. K-nearest neighbor classification further validated the clinico-anatomical correlates emphasizing the functional importance of identified neural substrates with area under the receiving operating characteristic curves (AUROC) between 0.67 - 0.91. Overall, they were able to localize acute effects of hypothalamic region stimulation to distinct tracts and nuclei within the hypothalamus and the wider diencephalon providing clinico-anatomical insights that may help to guide future neuromodulation work [1].

Cluster headache (CR) is the most severe human headache and is chronic in 10%-20% of patients, and 10% can become refractory to all effective drugs. In this scenario, surgical procedures are indicated:

see Sphenopalatine ganglion stimulation for cluster headache

see Occipital nerve stimulation for cluster headache.

Deep brain stimulation (DBS) of the posterior hypothalamus was found to be effective in the treatment of drug-resistant chronic cluster headache [2].

Case series

Bartsch et al. reported the results of a multicentre case series of six patients with chronic cluster headache in whom a DBS in the posterior hypothalamus was performed. Electrodes were implanted stereotactically in the ipsilateral posterior hypothalamus according to published coordinates 2 mm lateral, 3 mm posterior and 5 mm inferior referenced to the mid-AC-PC line. Microelectrode recordings at the target revealed single unit activity with a mean discharge rate of 17 Hz (range 13-35 Hz, n = 4). Out of six patients, four showed a profound decrease of their attack frequency and pain intensity on the visual analogue scale during the first 6 months. Of these, one patient was attack free for 6 months under neurostimulation before returning to the baseline which led to abortion of the DBS. Two patients had experienced only a marginal, non-significant decrease within the first weeks under neurostimulation before returning to their former attack frequency. After a mean follow-up of 17 months, three patients are almost completely attack free, whereas three patients can be considered as treatment failures. The stimulation was well tolerated and stimulation-related side-effects were not observed on long term. DBS of the posterior inferior hypothalamus is an effective therapeutic option in a subset of patients. Future controlled multicentre trials will need to confirm this open-label experience and should help to better define predictive factors for non-responders [3].

Hypothalamic deep brain stimulation: may respond to hypothalamic stimulation, but larger trials with longer follow-up are needed [4].

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