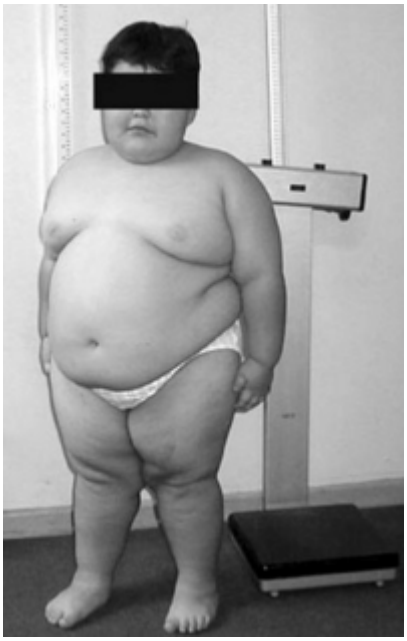
Prader–Willi syndrome



Prader–Willi syndrome (PWS) is a genetic disorder due to loss of function of specific genes.

In newborns, symptoms include weak muscles, poor feeding, and slow development.

Beginning in childhood, the person becomes constantly hungry, which often leads to obesity and type 2 diabetes.

Also, mild to moderate intellectual impairment and behavioral problems are typical.

Often, the forehead is narrow, hands and feet are small, height is short, skin is light in color, and most of the affected are unable to have children.

About 74% of cases occur when part of the father's chromosome 15 is deleted.

In another 25% of cases, the person has two copies of chromosome 15 from their mother and none from their father.

As parts of the chromosome from the mother are turned off, they end up with no working copies of certain genes.

PWS is not generally inherited, but instead the genetic changes happen during the formation of the egg, sperm, or in early development.

Franco et al., presented case series from the Hospital das Clínicas. Four patients with genetically confirmed Prader-Willi syndrome (PWS) presenting with severe obesity were included.

Deep brain stimulation electrodes were bilaterally implanted in the lateral hypothalamic area. After DBS implantation, the treatment included the following phases: titration (1-2 months), stimulation off (2 months), low-frequency DBS (40 Hz; 1 month), washout (15 days), high-frequency DBS (130 Hz; 1 month), and long-term follow-up (6 months).

Primary outcome measures were adverse events recorded during stimulation and long-term DBS treatment. Secondary outcomes consisted of changes in anthropometric measures (weight, body mass index [calculated as weight in kilograms divided by height in meters squared], and abdominal and neck circumference), bioimpedanciometry, and calorimetry after 6 months of treatment compared with baseline. The following evaluations and measurements were conducted before and after DBS: clinical, neurological, psychiatric, neuropsychological, anthropometry, calorimetry, blood workup, hormonal levels, and sleep studies. Adverse effects were monitored during all follow-up visits.

Four patients with PWS were included (2 male and 2 female; ages 18-28 years). Baseline mean (SD) body mass index was 39.6 (11.1). Two patients had previous bariatric surgery, and all presented with psychiatric comorbidity, which was well controlled with the use of medications. At 6 months after long-term DBS, patients had a mean 9.6% increase in weight, 5.8% increase in body mass index, 8.4% increase in abdominal circumference, 4.2% increase in neck circumference, 5.3% increase in the percentage of body fat, and 0% change in calorimetry compared with baseline. Also unchanged were hormonal levels and results of blood workup, sleep studies, and neuropsychological evaluations. Two patients developed stimulation-induced manic symptoms. Discontinuation of DBS controlled this symptom in 1 patient. The other required adjustments in medication dosage. Two infections were documented, 1 associated with skin picking.

Safety of lateral hypothalamic area stimulation was in the range of that demonstrated in patients with similar psychiatric conditions receiving DBS. In the small cohort of patients with PWS treated in the study, DBS was largely ineffective [1].

Lateral hypothalamic area (LHA) local field potentials (LFPs) were recorded in a Prader-Willi patient undergoing deep brain stimulation (DBS) for obesity. During hunger, exposure to food-related cues induced an increase in beta/low-gamma activity. In contrast, recordings during satiety were marked by prominent alpha rhythms. Based on these findings, Talakoub et al., delivered alpha-frequency DBS prior to and during food intake. Despite reporting an early sensation of fullness, the patient continued to crave food. This suggests that the pattern of activity in LHA may indicate hunger/satiety states in humans but attest to the complexity of conducting neuromodulation studies in obesity [2].

References

1)
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2)
Talakoub O, Paiva RR, Milosevic M, Hoexter MQ, Franco R, Alho E, Navarro J, Pereira JF Jr, Popovic MR, Savage C, Lopes AC, Alvarenga P, Damiani D, Teixeira MJ, Miguel EC, Fonoff ET, Batistuzzo MC, Hamani C. Lateral hypothalamic activity indicates hunger and satiety states in humans. Ann Clin Transl Neurol. 2017 Oct 20;4(12):897-901. doi: 10.1002/acn3.466. eCollection 2017 Dec. PubMed PMID: 29296618; PubMed Central PMCID: PMC5740250.