


NON-PHARMACOLOGICAL TREATMENT OF EPILEPSY

Klara Pintarić
University of Zagreb, School of Medicine

 0009-0001-7700-1496

Epilepsy, one of the world's oldest recognized conditions and fourth most common neurological disorder, is a disease characterized by a long-lasting predisposition to epileptic seizures. In around 70% of patients, epilepsy can be managed by common antiseizure drugs (ASD), either as a monotherapy or a combination of ASDs. The remaining 30% of patients, however, fail to achieve sustained seizure freedom even upon administration of a combination therapy of more than three drugs, rendering their epilepsy refractory or drug-resistant (DRE). Several possible mechanisms for this phenomenon have been proposed, such as the over-expression of multi-drug-resistant transporters responsible for drug efflux, modifications in ion channels or receptors, or epigenetic changes. In such cases, epilepsy surgery, when possible, is the next best step. However, if surgery is contraindicated, deep brain stimulation of the anterior nucleus of the thalamus (ANT-DBS) may be a reasonable alternative. Unfortunately, there is not enough data to justify the continuation of DBS during pregnancy, which is a condition that by itself eliminates several drug options due to their teratogenicity, further reducing the number of treatment options. Only 20 reported cases exist, and until recently, none included cyclic ANT-DBS. A study done by Patrick M. House and his colleagues

from the Hamburg Epilepsy Center is an exception to this rule. They treated two patients with ANT-DBS during pregnancy, delivery, and the postpartum period and reported their results.

Both patients had a history of frontal lobe epilepsy with hyperkinetic seizures since childhood, with unknown etiologies. After their epilepsies became drug-refractory, both underwent bilateral implantation of DBS electrodes into the anterior nucleus of the thalamus and mammillothalamic tract. Ten months after implantation (patient A) and 42 weeks later (patient B), contraception was discontinued. The patients became pregnant for the first time two and four months later respectively. At their explicit request, DBS was continued and ASDs were adapted to accommodate pregnancy. Patient A maintained stable seizure frequency whereas patient B experienced an initial increase, including a bilateral tonic-clonic seizure shortly before delivery. Ultimately, patient B's seizure control was down to one focal seizure every 2-3 months. The patients gave birth nine months later via Cesarean section, during which the DBS stimulation was paused. At a 6-month follow-up (patient B), and a two-year follow-up (patient A), both children were healthy. Seizure frequency in patient A remained stable, while patient B required an increase in

stimulation, experiencing focal seizures per month after which the seizure-frequency stabilized.

Even though there is still insufficient data present to recommend DBS continuation during pregnancy, there are now twenty-two documented pregnancies without complications and there are still no known potential risks for pregnancy or fertility. Still, given the fact that mammillary bodies of the hypothalamus, which are a part of the mammillothalamic tract stimulated by ANT-DBS, are a part of the hypothalamic-pituitary-ovarian axis, ANT-DBS might interfere with complex hormonal changes necessary to conceive and sustain pregnancy. This case shows that ANT-DBS did not prevent the patients from conceiving after only a few monthly cycles and even though the amplitude stimulation in patient B was increased, no negative effects on the patients or their children were observed. Given the small sample of studies published and the sensitive nature of pregnancy, which affects not only the mother but also the child, more research needs to be conducted in order to safely recommend ANT-DBS during pregnancy. For now, this approach to refractive epilepsy appears safe and might prove to be a good option for women suffering from epilepsy who wish to have children.

REFERENCES:

1. House PM, Herzer A, Lorenzi I, et al. Deep brain stimulation (DBS) of anterior nucleus thalami (ANT) in female epilepsy patients during pregnancy and delivery: experience from two cases. *Epileptic Disord.* 2021;23(6):933-936. doi:10.1684/epd.2021.1330