

Category:**Study type:**

Author's declarative title: Thalamotomy using MRI-guided focused ultrasound significantly improves contralateral symptoms and quality of life in essential tremor

Citation: Elias WJ, Lipsman N, Ondo WG, et al. A Randomized Trial of Focused Ultrasound Thalamotomy for Essential Tremor. *N Engl J Med.* 2016 Aug 25;375(8):730-9.

Commentary (794 words starting from context)**Context**

Propranolol and primidone significantly reduce tremor by around 60% in 50% of essential tremor (ET) patients. When medication is ineffective or causes intolerable side effects, neurosurgical intervention may be considered. Until recently, radiofrequency (RF) ablation or deep brain stimulation (DBS) of the ventralis intermedius (VIM) thalamic nucleus were the main surgical options. Gamma knife thalamotomy avoids a burrhole but delayed effects make intraoperative validation impossible(1). Recent technical advances have enabled transcranial delivery of high-intensity focused ultrasound to create a thalamotomy with magnetic resonance imaging (MRI) guidance and real-time monitoring. Previous uncontrolled studies suggested that this may be a safe and effective alternative for ET patients(2).

Methods

This randomized controlled trial examined the effect of unilateral focused ultrasound thalamotomy or a sham procedure (in a 3:1 ratio) on hand tremor. The primary outcome was the between-group difference in hand tremor change from baseline to 3 months after intervention as measured with the Clinical Rating Scale for Tremor (CRST). Video recordings were rated by independent blinded neurologists. Quality of Life in ET questionnaires (QUEST) were also completed. Adverse effects were meticulously recorded.

Findings

Seventy-six patients (71±8 years) were included. The primary outcome was significantly different between groups with 47% improvement (18±5 to 10±5) in contralateral hand tremor in the active and 0% (16±4 to 16±5) in the sham group (95%CI, 6 to 11; P<0.001). This was clinically relevant with 62% vs. 3% reduction in CRST disability scores (P<0.001) and 46% vs. 3% reduction in QUEST scores (P<0.001). The commonest adverse events were gait disturbance and paraesthesia, each affecting around 1/3 of patients. Persistent severe adverse events occurred in 3 of 56 actively treated patients (contralateral weakness, dense hypoesthesia and ataxia requiring a walker for ambulation).

Commentary

This well-designed double-blind multicentre trial took full advantage of the ability to perform a sham intervention with MRI-guided focused ultrasound. It demonstrated significant improvement in contralateral symptoms, disability scores and quality of life. No other surgical therapy for ET has been evaluated with such scientific rigour.

Haemorrhage leading to death or disability is a rare complication of DBS and RF thalamotomy, although the risk is much less than 1% when employing an image-verified approach(3). Patients averse to invasive surgery may consider gamma knife or focused ultrasound techniques. The latter requires a full head shave and current technology limitations may result in failure to make significant thermal lesions in a proportion of patients(4). Although a surgical incision is not required, thalamic lesioning carries a risk of persistent neurological deficit. As with other surgical interventions, there was a slight decline in symptomatic efficacy over time but without impacting quality of life scores.

DBS for movement disorders was initially popularised by VIM stimulation contralateral to a prior RF thalamotomy and was driven by the desire to reduce the high incidence of side effects when performing bilateral thalamotomy(5). Thalamic stimulation has fewer adverse effects and results in greater functional improvement than RF thalamotomy, although tolerance undermines its efficacy advantage after 5 years(6). The main advantage of DBS is the potential for bilateral intervention. Nevertheless, hardware infection and malfunction may result in therapeutic withdrawal and symptom rebound(7).

Implications for practice

This study expands the number of surgical therapies available to medically refractory ET patients. Future long-term comparative studies may provide further data on relative efficacy and side effect profile of these different surgical approaches. However, technical limitations, patient preference, local availability and expertise may ultimately determine which modality is used in individual patients.

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Competing interests

None