Randomised, Double-Blinded, Multi-Centre, Placebo-Controlled Trial of Deep Brain Stimulation for Essential Tremor

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Introduction

Deep brain stimulation (DBS) for intractable essential tremor (ET) has yet to be evaluated by a randomised placebo-controlled trial. We applied three statistical methods to evaluate DBS efficacy in ET: 1) traditional randomised prospective cohort analysis; 2) N-of-1 single patient randomised control trials; 3) Signal-to-noise (S2N) analysis (1).

Methods

ET patients receiving thalamic or zona incerta stimulation were studied. Stimulation was switched -off and maximal tremor severity (2) reached. Stimulation was randomly programmed On unilaterally or Off (placebo) with patient and tremor evaluator blinded. When tremor severity had declined more than 80%, the timed trial was stopped. Patients reported whether they perceived stimulation to be On or not. 6 pairs of trials were performed.

Results

21 patients were studied, mean age 67.6 years, mean tremor duration 382.7 months and time since surgery 1186 days.

1) Mean time until tremor attenuation was 25.3 seconds (SD+71.9) On versus 126.3 seconds (SD+75.6) Off, z=-3.808, p<0.0005. Mean end-of-trial tremor severity was 0.84 (SD+0.75) On and 6.62 (SD+1.87) Off, t=-13.218, p<0.0005.

2) N-of-1: Mean number of correct perceptions was 11.2/12, a probability of p<0.030. 60% of patients had 12 correct perceptions (p=0.001), 20% had 11 correct perceptions (p=0.013). Within each patient, tremor severity was better On versus Off, significant (p<0.05) in 78.9% of patients.

3) S2N: Mean S2N ratio was >10 (i.e. significant) in 100% of 19 patients trialled On (mean 356,927,124, SD+289,004,393) versus 11% of patients Off (mean 44,026,220, SD+38,370,349). Average chance of >80% ET improvement without DBS was therefore <1/350miliion (range 1/ 70 million to 1/1009 million).

Conclusions

This is the first randomised, placebo-controlled trial of DBS for ET and demonstrates a large treatment effect. N-of-1 and S2N are therefore important, valid, cost-effective alternatives to large trials for proving benefit in patients receiving neurosurgery.

Learning Objectives

By the conclusion of this session, participants should be able to:

1) Describe N-of-1 and Signal-to-Noise trials.

2) Appreciate the potential application of these types of trials in the cost-effective evaluation of efficacy of surgical procedures in which a large treatment effect exists.

3) Describe the efficacy of DBS in the treatment of ET.

References

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2. Bain PG, Findley LJ, Atchinson P, Behari M, Vidailhet M, Gresty M, Rothwell JC, Thompson PD, Marsden CD. Assessing tremor severity. J Neurology Neurosurgery Psychiatry 1993;56:868-73.

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