CONCLUSIONS

- Tolerance to deep brain stimulation (DBS) can be described as:
  1. tremor rebound with a temporary increase of tremor intensity over the preoperative state after switching off DBS (Kronenbeger 2009).
  2. habituation, which is the loss of sustained tremor control over a short duration of follow-up (Barbe 2011), or
  3. late therapy failure that may occur after at least one year of satisfactory control of tremor with DBS (Pilitsis 2008).

- Causes not completely understood. There include:
  - Natural disease progression
  - Inadequate electrode location
  - Resolution of microhalothamyotomy effects from surgery
  - Adaptation of neural networks to chronic localized stimulation (Barbe 2011).

- Existing research shows:
  - 13-40% of patients with essential tremor (ET) implanted in the thalamus (VM) develop tolerance, despite proper lead placement (Pilitsis et al., 2008).
  - A prospective study found 73% of ET patients experienced waning benefit of stimulation, as early as 3 months following implantation (Shih et al., 2013).
  - Loss of acute benefit from programming in 54% of electrodes in ET patients with VM stimulation by 10 weeks (Barbe et al., 2011).
  - Rebound is described in ET and Parkinson’s disease (PD) (Hantz et al., 2009) but is not well-characterized.

- Objective: To determine factors and characteristics associated with development of tolerance to DBS across disease states and targets.

METHODS

- Prospective questionnaire study with retrospective chart review in a 3-month cross-sectional population of a tertiary Movement Disorders Center.
- Inclusion criteria:
  - > 18 years old
  - diagnosis of ET, PD, or dystonia as determined by a movement disorder specialist.
  - lead implantation in the VM, globus pallidus interna (GPi), or the subthalamic nucleus (STN).
- Exclusion criteria:
  - Stimulator in place < 6 months
- Prospective evaluation included a Clinician-administered survey to identify diagnosis, disease onset, stimulator placement date, target and laterality for all patients who agreed to complete surveys.
- Retrospective chart review to identify diagnosis, disease onset, stimulator placement date, target and laterality for all patients who agreed to complete surveys.
- Information was extracted to a database for analysis. Statistical methods included 2-tailed Fisher’s exact test to compare incidence of tolerance across disease states and targets. Mann Whitney U to compare self-report measures in patients with and without tolerance. Kruskal-Wallis and ANOVA* to compare self-report measures among those experiencing tolerance across disease states and targets, and 2-tailed t-test to compare patient characteristics.

RESULTS

- Table 1: Patient Characteristics
  - Gender
  - M: 14
  - F: 9
  - Analysis by disease state:
    - 25.6% (n = 11) PD
    - 56.3% (n = 9) ET
    - 20% (n = 2) dystonia
    - (P = 0.004)*
  - Analysis by target:
    - 32.3% (n = 11) STN
    - 52.6% (n = 10) VM
    - 6.3% (n = 1) GPi
    - (P = 0.011)*
  - Analysis by disease state by target:
    - 20.6% (n = 7) STN
    - 47.4% (n = 9) VM
    - 18.8% (n = 3) GPi
    - (P = 0.010)*
  - *2-tailed Fisher’s exact test

- Table 2: Characteristics of patients experiencing habituation
  - Mean age (years) at time of survey
  - Mean disease duration (years) at time of survey
  - Mean time (years) since DBS at time of survey
  - Time of survey
  - Analysis by disease state:
    - 25.6% (n = 11) PD
    - 56.3% (n = 9) ET
    - 20% (n = 2) dystonia
    - (P = 0.004)*
  - Analysis by target:
    - 32.3% (n = 11) STN
    - 52.6% (n = 10) VM
    - 6.3% (n = 1) GPi
    - (P = 0.011)*
  - Analysis by disease state by target:
    - 20.6% (n = 7) STN
    - 47.4% (n = 9) VM
    - 18.8% (n = 3) GPi
    - (P = 0.010)*
  - *2-tailed Fisher’s exact test

- Table 3: Characteristics of patients experiencing rebound
  - Mean age (years) at time of survey
  - Mean disease duration (years) at time of survey
  - Mean time (years) since DBS at time of survey
  - Time of survey
  - Analysis by disease state:
    - 25.6% (n = 11) PD
    - 56.3% (n = 9) ET
    - 20% (n = 2) dystonia
    - (P = 0.004)*
  - Analysis by target:
    - 32.3% (n = 11) STN
    - 52.6% (n = 10) VM
    - 6.3% (n = 1) GPi
    - (P = 0.011)*
  - Analysis by disease state by target:
    - 20.6% (n = 7) STN
    - 47.4% (n = 9) VM
    - 18.8% (n = 3) GPi
    - (P = 0.010)*
  - *2-tailed Fisher’s exact test

- Table 4: Patient self-report measures on efficacy, satisfaction, and global impression of change with DBS in patients reporting habituation by stimulator target
  - Overall efficacy of DBS
  - Overall satisfaction with DBS
  - Patient global impression of change
  - + rebound
  - *2-tailed Fisher’s exact test

- Table 5: Patient self-report measures on efficacy, satisfaction, and global impression of change with DBS in patients reporting rebound by stimulator target
  - Overall efficacy of DBS
  - Overall satisfaction with DBS
  - Patient global impression of change
  - + rebound
  - *2-tailed Fisher’s exact test

REFERENCES


Clinical Manifestations of Tolerance to Deep Brain Stimulation

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